Access DB# 65124

SEARCH REQUEST FORM

Scientific and Technical Inf rmation Center

Requester's Full Name: S. Kumar Examiner #: 69594 Date: 11/28/02
Art Unit: 1621 Phone Number 30 8459 Serial Number: 09/776,936
Mail Box and Bldg/Room Location: CM1 7A07 7E12 Results Format Preferred (circle): PAPER DISK E-MAIL

If more than one search is submitted, please prioritize searches in order of need.

****

Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc, if known. Please attach a copy of the cover sheet, pertinent claims, and abstract.

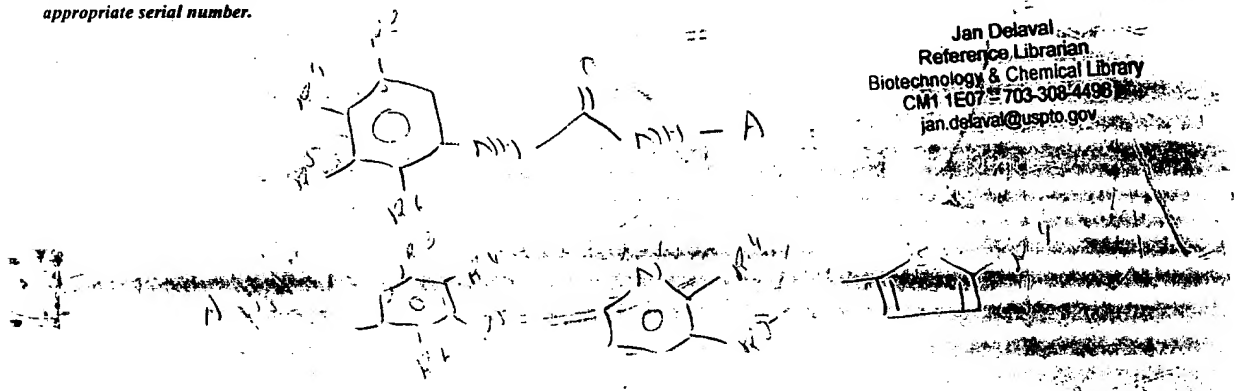
Title of Invention: Inhibitors of the [illegible] kinase

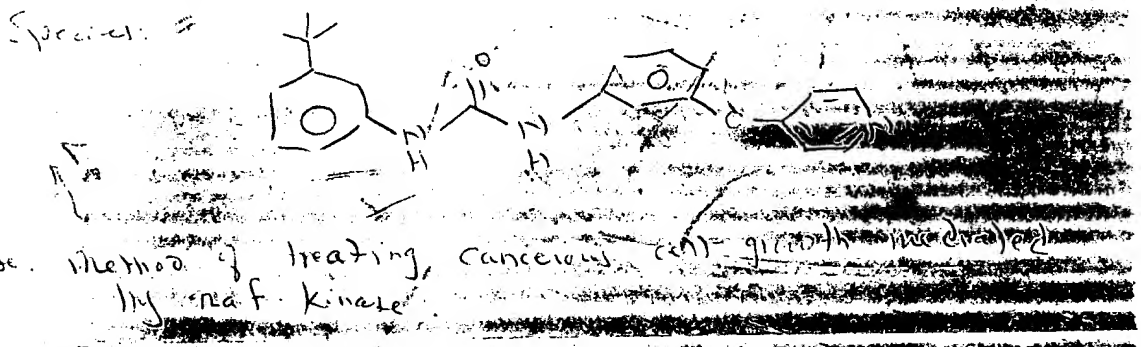
Inventors (please provide full names): Scott Miller et al

Earliest Priority Filing Date: 12/22/1997

For Sequence Searches Only *Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.*

Jan Delaval
Reference Librarian
Biotechnology & Chemical Library
CM1 1E07 - 703-308-4498
jan.delaval@uspto.gov





Use: Method of treating cancer(s) mediated by [illegible] kinase

****

STAFF USE ONLY

Searcher: _____
Searcher Phone #: 4498
Searcher Location: _____
Date Searcher Picked Up: 5/2/01
Date Completed: 5/2/01
Searcher Prep & Review Time: _____
Clerical Prep Time: 20
Online Time: + 80

Type of Search

NA Sequence (#) _____
AA Sequence (#) _____
Structure (#) ✓
Bibliographic _____
Litigation _____
Fulltext _____
Patent Family _____
Other _____

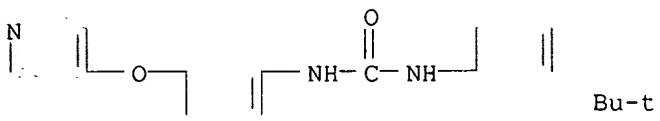
Vendors and cost where applicable

STN ✓
Dialog _____
Questel/Orbit _____
Dr.Link _____
Lexis/Nexis _____
Sequence Systems _____
WWW/Internet _____
Other (specify) _____

PTO-1590 (8-01)

Jan Delaval
Reference Librarian
Biotechnology & Chemical Library
CM1 1E07 – 703-308-4498
jan.delaval@uspto.gov

```
=> d his

     (FILE 'HOME' ENTERED AT 09:24:44 ON 02 MAY 2002)
               SET COST OFF

     FILE 'REGISTRY' ENTERED AT 09:25:11 ON 02 MAY 2002
L1            62 S C22H23N3O2/MF AND 46.150.18/RID AND NC5/ES AND 3/NR
L2             9 S L1 AND UREA
L3             2 S L2 AND DIMETHYLETHYL PHENYL
                 SEL RN
L4             0 S E1-E2/CRN

     FILE 'HCAOLD' ENTERED AT 09:26:26 ON 02 MAY 2002
L5             0 S L3

     FILE 'HCAPLUS' ENTERED AT 09:26:32 ON 02 MAY 2002
L6             1 S L3

     FILE 'USPATFULL, USPAT2' ENTERED AT 09:26:36 ON 02 MAY 2002
L7             0 S L3

=> fil reg
FILE 'REGISTRY' ENTERED AT 09:42:38 ON 02 MAY 2002
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2002 American Chemical Society (ACS)

STRUCTURE FILE UPDATES:   30 APR 2002  HIGHEST RN 409303-45-3
DICTIONARY FILE UPDATES:  30 APR 2002  HIGHEST RN 409303-45-3

TSCA INFORMATION NOW CURRENT THROUGH July 7, 2001

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

Crossover limits have been increased.  See HELP CROSSOVER for details.

Calculated physical property data is now available.  See HELP PROPERTIES
for more information.  See STNote 27, Searching Properties in the CAS
Registry File, for complete details:
http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf

=> d l3 ide can tot

L3   ANSWER 1 OF 2  REGISTRY  COPYRIGHT 2002 ACS
RN   228399-53-9  REGISTRY
CN   Urea, N-[3-(1,1-dimethylethyl)phenyl]-N'-[3-(4-pyridinyloxy)phenyl]-
     (9CI)  (CA INDEX NAME)
FS   3D CONCORD
MF   C22 H23 N3 O2
SR   CA
LC   STN Files:   CA, CAPLUS, TOXCENTER
```

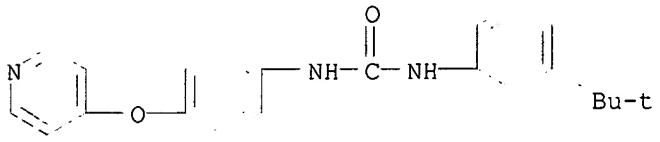



```
**PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT**
```

1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 131:58658

L3 ANSWER 2 OF 2 REGISTRY COPYRIGHT 2002 ACS
RN 228399-50-6 REGISTRY
CN **Urea, N-[3-(1,1-dimethylethyl)phenyl]-N'-[4-(4-pyridinyloxy)phenyl]-(9CI)** (CA INDEX NAME)
FS 3D CONCORD
MF **C22 H23 N3 O2**
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 131:58658

=> fil hcaplus
FILE 'HCAPLUS' ENTERED AT 09:42:46 ON 02 MAY 2002
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

FILE COVERS 1907 - 2 May 2002 VOL 136 ISS 18
FILE LAST UPDATED: 30 Apr 2002 (20020430/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

CAS roles have been modified effective December 16, 2001. Please check your SDI profiles to see if they need to be revised. For information on CAS roles, enter HELP ROLES at an arrow prompt or use the CAS Roles thesaurus (/RL field) in this file.

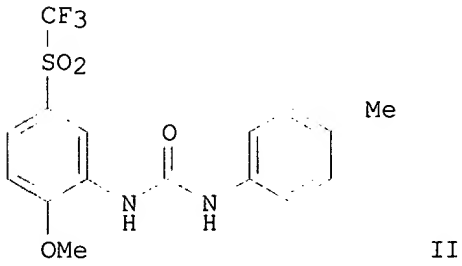
=> d all 16

L6 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2002 ACS

AN 1999:421642 HCAPLUS
DN 131:58658
TI Inhibition of raf kinase using symmetrical and unsymmetrical substituted diphenyl ureas
IN Miller, Scott; Osterhout, Martin; Dumas, Jacques; Khire, Uday; Lowinger, Timothy Bruno; Riedl, Bernd; Scott, William J.; Smith, Roger A.; Wood, Jill E.; Gunn, David; Rodriguez, Mareli; Wang, Ming
PA Bayer Corporation, USA
SO PCT Int. Appl., 89 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM C07C275-24
ICS C07D213-02; C07D333-02; A61K031-17; A61K031-38; A61K031-44
CC 25-21 (Benzene, Its Derivatives, and Condensed Benzenoid Compounds)
Section cross-reference(s): 1, 7
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9932436	A1	19990701	WO 1998-US26081	19981222
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	CA 2315646	AA	19990701	CA 1998-2315646	19981222
	AU 9919054	A1	19990712	AU 1999-19054	19981222
	EP 1049664	A1	20001108	EP 1998-963809	19981222
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	JP 2001526258	T2	20011218	JP 2000-525373	19981222
	NO 2000003230	A	20000821	NO 2000-3230	20000621
PRAI	US 1997-996344	A	19971222		
	WO 1998-US26081	W	19981222		

OS MARPAT 131:58658
GI



II

AB The invention relates to the use of a group of aryl ureas ANHCONHB [I; A = certain (un)substituted Ph, pyridinyl, or thien-2-yl groups; B = certain (un)substituted mono- to tricyclic aryl or heteroaryl groups] in treating raf-mediated diseases, and pharmaceutical compns. for use in such therapy. A subset of I are novel and are claimed per se. Approx. 160 invention compds. and numerous intermediates were prepd. For instance, reaction of tolyl isocyanate with 2-methoxy-5-(trifluoromethanesulfonyl)aniline in EtOAc gave title compd. II. In an in vitro raf kinase assay, all compds.

displayed IC50 values between 1 nM and 10 .mu.M.

ST diphenyl urea prepn raf kinase inhibitor; aryl urea prepn antitumor agent

IT Antitumor agents
(Inhibition of raf kinase using sym. and unsym. substituted di-Ph ureas)

IT Phosphoproteins
RL: BPR (Biological process); BSU (Biological study, unclassified); MSC (Miscellaneous); BIOL (Biological study); PROC (Process)
(gene c-raf; Inhibition of raf kinase using sym. and unsym. substituted di-Ph ureas)

IT 726-17-0P 780-90-5P 843-06-1P 883-62-5P 885-87-0P 5651-77-4P
6337-24-2P 13041-60-6P 13472-85-0P 16588-75-3P 18994-90-6P
27692-74-6P 28232-52-2P 31465-36-8P 32361-76-5P 36089-89-1P
40299-87-4P 51834-97-0P 61500-87-6P 62248-47-9P 62248-51-5P
64064-63-7P 67291-63-8P 70991-08-1P 92575-23-0P 116289-71-5P
135680-03-4P 142596-52-9P 165256-89-3P 178809-75-1P 220000-87-3P
228401-08-9P 228401-09-0P 228401-10-3P 228401-11-4P 228401-14-7P
228401-15-8P 228401-16-9P 228401-17-0P 228401-18-1P 228401-19-2P
228401-20-5P 228401-21-6P 228401-22-7P 228401-23-8P 228401-24-9P
228401-26-1P 228401-27-2P 228401-28-3P 228401-29-4P 228401-31-8P
228401-32-9P 228401-33-0P 228401-34-1P 228401-35-2P 228401-36-3P
228401-37-4P 228401-38-5P 228401-39-6P 228401-40-9P 228401-41-0P
228401-43-2P 228401-44-3P 228401-45-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; prepn. of sym. and unsym. substituted di-Ph ureas with inhibitory effects on tumors mediated by raf kinase)

IT 370-50-3P 228399-32-4P 228399-33-5P 228399-34-6P 228399-35-7P
228399-36-8P 228399-38-0P 228399-39-1P 228399-40-4P 228399-41-5P
228399-42-6P 228399-43-7P 228399-44-8P 228399-45-9P 228399-47-1P
228399-48-2P 228399-49-3P **228399-50-6P** 228399-51-7P
228399-52-8P **228399-53-9P** 228399-54-0P 228399-56-2P
228399-57-3P 228399-58-4P 228399-59-5P 228399-60-8P 228399-61-9P
228399-62-0P 228399-63-1P 228399-65-3P 228399-66-4P 228399-67-5P
228399-68-6P 228399-69-7P 228399-70-0P 228399-71-1P 228399-72-2P
228399-74-4P 228399-75-5P 228399-76-6P 228399-77-7P 228399-78-8P
228399-79-9P 228399-80-2P 228399-82-4P 228399-83-5P 228399-84-6P
228399-85-7P 228399-86-8P 228399-87-9P 228399-88-0P 228399-89-1P
228399-90-4P 228399-92-6P 228399-93-7P 228399-94-8P 228399-95-9P
228399-96-0P 228399-97-1P 228399-98-2P 228399-99-3P 228400-01-9P
228400-02-0P 228400-03-1P 228400-04-2P 228400-05-3P 228400-06-4P
228400-07-5P 228400-08-6P 228400-10-0P 228400-11-1P 228400-12-2P
228400-13-3P 228400-14-4P 228400-15-5P 228400-16-6P 228400-17-7P
228400-18-8P 228400-20-2P 228400-21-3P 228400-22-4P 228400-23-5P
228400-24-6P 228400-25-7P 228400-26-8P 228400-27-9P 228400-28-0P
228400-30-4P 228400-31-5P 228400-32-6P 228400-33-7P 228400-34-8P
228400-35-9P 228400-36-0P 228400-37-1P 228400-38-2P 228400-39-3P
228400-40-6P 228400-41-7P 228400-42-8P 228400-43-9P 228400-44-0P
228400-45-1P 228400-46-2P 228400-47-3P 228400-48-4P 228400-49-5P
228400-50-8P 228400-51-9P 228400-52-0P 228400-53-1P 228400-54-2P
228400-55-3P 228400-56-4P 228400-57-5P 228400-58-6P 228400-60-0P
228400-61-1P 228400-62-2P 228400-63-3P 228400-64-4P 228400-65-5P
228400-66-6P 228400-67-7P 228400-69-9P 228400-70-2P 228400-71-3P
228400-72-4P 228400-73-5P 228400-74-6P 228400-75-7P 228400-76-8P
228400-77-9P 228400-78-0P 228400-79-1P 228400-80-4P 228400-81-5P
228400-82-6P 228400-83-7P 228400-84-8P 228400-85-9P 228400-87-1P
228400-89-3P 228400-91-7P 228400-92-8P 228400-93-9P 228400-94-0P
228400-95-1P 228400-96-2P 228400-97-3P 228400-99-5P 228401-00-1P
228401-01-2P 228401-02-3P 228401-03-4P 228401-04-5P 228401-06-7P
228401-07-8P 228401-49-8P 228401-50-1P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of sym. and unsym. substituted di-Ph ureas with inhibitory effects on tumors mediated by raf kinase)
IT 144378-33-6, Raf Kinase
RL: BPR (Biological process); BSU (Biological study, unclassified); MSC (Miscellaneous); BIOL (Biological study); PROC (Process)
(prepn. of sym. and unsym. substituted di-Ph ureas with inhibitory effects on tumors mediated by raf kinase)
IT 86-84-0, 1-Naphthyl isocyanate 100-11-8, 4-Nitrobenzyl bromide 100-15-2, N-Methyl-4-nitroaniline 100-51-6, Benzyl alcohol, reactions 101-77-9 106-44-5, reactions 106-49-0, p-Toluidine, reactions 108-30-5, reactions 109-00-2, 3-Hydroxypyridine 110-91-8, Morpholine, reactions 123-30-8, 4-Aminophenol 150-76-5, 4-Methoxyphenol 288-32-4, Imidazole, reactions 320-94-5, 2-Nitro-4-(trifluoromethyl)benzoic acid 327-78-6, 4-Chloro-3-(trifluoromethyl)phenyl isocyanate 349-65-5, 2-Methoxy-5-(trifluoromethyl)aniline 350-46-9, 1-Fluoro-4-nitrobenzene 358-23-6, Trifluoromethanesulfonic anhydride 371-40-4, 4-Fluoroaniline 400-74-8, 2-Fluoro-5-nitrobenzotrifluoride 452-80-2, 2-Fluoro-4-methylaniline 453-20-3, 3-Hydroxytetrahydrofuran 498-74-8, 4-Methoxymetanilyl fluoride 551-06-4 585-34-2 585-79-5, 1-Bromo-3-nitrobenzene 620-95-1, 3-Benzylpyridine 622-58-2, p-Tolyl isocyanate 624-28-2, 2,5-Dibromopyridine 626-61-9, 4-Chloropyridine 768-35-4 872-31-1, 3-Bromothiophene 883-99-8 1083-48-3, 4-(4-Nitrobenzyl)pyridine 1121-78-4, 5-Hydroxy-2-methylpyridine 1849-36-1 2033-89-8, 3,4-Dimethoxyphenol 2103-88-0, 2-Mercapto-4-phenylthiazole 3279-07-0, 4-tert-Butyl-2-nitrophenol 3535-88-4, 5-tert-Butyl-2-methoxyaniline 3678-63-5 4548-45-2, 2-Chloro-5-nitropyridine 4556-23-4, 4-Mercaptopyridine 4595-59-9, 5-Bromopyrimidine 6310-19-6, 4-tert-Butyl-2-nitroaniline 6358-07-2 7379-35-3, 4-Chloropyridine hydrochloride 21101-60-0, 4-(4-Nitrophenylthio)phenol 22948-02-3, 3-Aminothiophenol 24424-99-5, Di-tert-butyl dicarbonate 25267-27-0, Iodobutane 29264-35-5 36265-31-3 73322-01-7, 4-(2-Pyridinylthio)-1-nitrobenzene 198077-72-4, 2-Methoxy-5-(difluoromethanesulfonyl)aniline 228401-47-6, 2,4-Dimethoxy-5-(trifluoromethyl)aniline 228401-48-7, 2-Hydroxy-5-(trifluoromethylthio)aniline
RL: RCT (Reactant); RACT (Reactant or reagent)
(reactant; prepn. of sym. and unsym. substituted di-Ph ureas with inhibitory effects on tumors mediated by raf kinase)
RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) Dixon; US 5470882 A 1995 HCAPLUS
(2) Seto; US 5429918 A 1995 HCAPLUS
(3) Smithkline Beecham Corporation; WO 96/25157 A1 1996 HCAPLUS

=> fil reg
FILE 'REGISTRY' ENTERED AT 11:14:47 ON 02 MAY 2002
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

STRUCTURE FILE UPDATES: 30 APR 2002 HIGHEST RN 409303-45-3
DICTIONARY FILE UPDATES: 30 APR 2002 HIGHEST RN 409303-45-3

TSCA INFORMATION NOW CURRENT THROUGH July 7, 2001

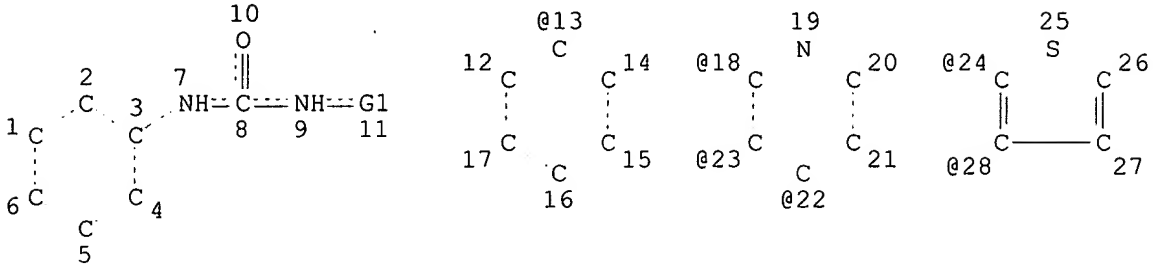
Please note that search-term pricing does apply when conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Calculated physical property data is now available. See HELP PROPERTIES for more information. See STNote 27, Searching Properties in the CAS

Registry File, for complete details:
http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf

```
=> d sta que l2
L1              STR
```




```
VAR G1=13/18/23/22/24/28
NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS  28

STEREO ATTRIBUTES: NONE
L2        23426 SEA FILE=REGISTRY SSS FUL L1

100.0% PROCESSED  75223 ITERATIONS                      23426 ANSWERS
SEARCH TIME: 00.00.06


=> d his

     (FILE 'HOME' ENTERED AT 10:57:31 ON 02 MAY 2002)
               SET COST OFF

     FILE 'REGISTRY' ENTERED AT 10:57:51 ON 02 MAY 2002
               ACT KUMAR776/A
              ---------
L1             STR
L2        23426 SEA FILE=REGISTRY SSS FUL L1
              ---------
L3            2 S L2 AND C22H23N3O2/MF
L4        23424 S L2 NOT L3

     FILE 'HCAPLUS' ENTERED AT 10:58:50 ON 02 MAY 2002
L5         8315 S L4

     FILE 'REGISTRY' ENTERED AT 11:00:54 ON 02 MAY 2002
L6            1 S 144378-33-6

     FILE 'HCAPLUS' ENTERED AT 11:01:43 ON 02 MAY 2002
L7          297 S L6
L8          546 S RAF KINASE OR C RAF KINASE OR PROTEIN KINASE C RAF OR GENE C
L9           17 S KINASE PHOSPHORYLATING GENE C RAF PROTEIN
L10         574 S L7-L9
L11           7 S L5 AND L10

     FILE 'REGISTRY' ENTERED AT 11:03:31 ON 02 MAY 2002
L12           11 S (L8 OR L9) NOT L6
```

```
     FILE 'HCAPLUS' ENTERED AT 11:04:15 ON 02 MAY 2002
L13          143 S L12
L14            1 S L5 AND L13
L15            7 S L11,L14
L16         6950 S L5 AND (PY<=1997 OR PRY<=1997 OR AY<=1997)
L17            5 S L15 AND L16
                 E BAYER/PA,CS
L18          197 S E3,E4 AND L5
                 E MILLER S/AU
L19          930 S E3-E36
                 E  MILLER SCOTT/AU
L20          222 S E3-E26
                 E OSTERHOUT M/AU
L21           34 S E3-E5,E7-E9
                 E DUMAS J/AU
L22          458 S E3-E16
                 E KHIRE U/AU
L23           24 S E4-E6
                 E LOWINGER T/AU
L24           23 S E4-E6
                 E RIEDL B/AU
L25           84 S E3,E7
                 E SCOTT W/AU
L26          155 S E3,E22-E27
                 E SCOTT WILL/AU
L27          153 S E3,E34-E39
                 E SMITH R/AU
L28          992 S E3-E15
                 E SMITH ROGER/AU
L29          219 S E3-E7
                 E WOOD J/ AU
L30          178 S E3,E16-E20
                 E WOOD JILL/AU
L31           14 S E3-E5
                 E GUNN D/AU
L32           33 S E3,E6,E15,E16
                 E RODRIGUEZ M/AU
L33          942 S E3-E70,E242-E251
                 E WANG M/AU
L34         1245 S E3-E34
                 E WANG MING/AU
L35         2083 S WANG MING?/AU
                 E TURNER T/AU
L36          358 S E3-E23
                 E TURNER TIFFANY/AU
L37            1 S E3
                 E BRENNAN C/AU
L38           74 S E3-E13,E21-E25
L39           18 S L5 AND L19-L38
L40           10 S L16 AND L39
                 E GUNN DAVID/AU
L41           10 S E3
L42            3 S L41 AND L5
L43            2 S RODRIGUEZ M?/AU AND L5
L44            7 S L39,L42,L43,L18 AND L15
L45            5 S L16 AND L44
L46            2 S L44 NOT L45

     FILE 'REGISTRY' ENTERED AT 11:14:47 ON 02 MAY 2002

=> fil hcaplus
FILE 'HCAPLUS' ENTERED AT 11:15:08 ON 02 MAY 2002
```

FILE COVERS 1907 - 2 May 2002 VOL 136 ISS 18
FILE LAST UPDATED: 30 Apr 2002 (20020430/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

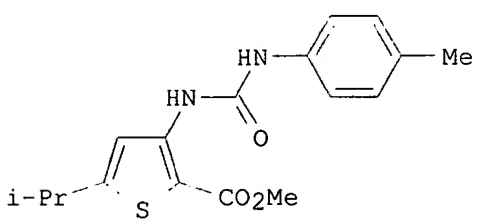
CAS roles have been modified effective December 16, 2001. Please check your SDI profiles to see if they need to be revised. For information on CAS roles, enter HELP ROLES at an arrow prompt or use the CAS Roles thesaurus (/RL field) in this file.

=> d l45 bib abs hitrn tot

L45 ANSWER 1 OF 5 HCAPLUS COPYRIGHT 2002 ACS
AN 2001:111513 HCAPLUS
DN 134:163040
TI Preparation of heteroaryl aryl ureas as **raf kinase** inhibitors
IN **Wood, Jill E.**; Wild, Hanno; Rogers, Daniel H.; Lyons, John; Katz, Michael; Caringal, Yolanda; Dally, Robert; Lee, Wendy; **Smith, Roger A.**; Blum, Cheri
PA Onyx Pharmaceuticals, USA; **Bayer** Corporation
SO U.S., 30 pp.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE		APPLICATION NO.	DATE	
PI	US 6187799	B1	20010213		US 1998-83399	19980522	<--
	US 2001006975	A1	20010705		US 2001-755060	20010108	
PRAI	US 1997-126420P	P	19970523	<--			
	US 1998-83399	A3	19980522				

GI



I

AB The title heteroaryl aryl ureas, useful in treating tumors mediated by

raf kinase (no data), were prepd. E.g., a multi-step synthesis of the urea I was given. The title compds. such as I are effective at 0.01-200 mg/kg/day.

IT **216573-01-2P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(prepn. of heteroaryl aryl ureas as **raf kinase** inhibitors)

IT **216573-03-4P 216573-34-1P 216574-09-3P 216574-10-6P 216574-11-7P 216589-05-8P 216589-46-7P 216852-73-2P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of heteroaryl aryl ureas as **raf kinase** inhibitors)

IT **144378-33-6, RAF kinase**
RL: BSU (Biological study, unclassified); MSC (Miscellaneous); BIOL (Biological study)
(prepn. of heteroaryl aryl ureas as **raf kinase** inhibitors)

IT **216591-27-4P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of heteroaryl aryl ureas as **raf kinase** inhibitors)

RE.CNT 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

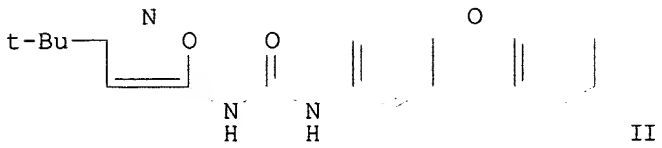
L45 ANSWER 2 OF 5 HCAPLUS COPYRIGHT 2002 ACS
AN 1999:425740 HCAPLUS
DN 131:73648
TI Inhibition of **raf kinase** using substituted heterocyclic ureas
IN **Dumas, Jacques; Khire, Uday; Lowinger, Timothy Bruno**; Paulsen, Holger; **Riedl, Bernd; Scott, William J.; Smith, Roger A.; Wood, Jill E.**; Hatoum-Mokdad, Holia; Johnson, Jeffrey; Lee, Wendy; Redman, Aniko
PA **Bayer** Corporation, USA
SO PCT Int. Appl., 163 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9932106	A1	19990701	WO 1998-US26078	19981222 <--
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	CA 2315717	AA	19990701	CA 1998-2315717	19981222 <--
	AU 9921989	A1	19990712	AU 1999-21989	19981222 <--
	EP 1047418	A1	20001102	EP 1998-965981	19981222 <--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	JP 2001526220	T2	20011218	JP 2000-525097	19981222 <--

	NO 2000003232	A	20000821	NO 2000-3232	20000621 <--
PRAI	US 1997-996343	A	19971222 <--		
	WO 1998-US26078	W	19981222		

OS MARPAT 131:73648

GI



II

AB A method for treatment of cancerous cell growth mediated by **raf kinase** comprises administration of urea derivs. ANHCONHB [I; A = substituted isoxazolyl, thienyl, thiadiazolyl, furyl, pyrazolyl, etc.; B = (substituted) mono-, di-, or tricyclic aryl, heteroaryl contg. .gtoreq.1 5-6 membered arom. structure contg. 0-4 N, O, or S atoms]. Reaction of 4-phenyloxyphenyl isocyanate with 5-amino-3-tert-butylisoxazole in methylene chloride and heating at reflux temp. for 2 days gave title compd. II. In an in vitro **raf kinase** assay, I displayed IC50 values of 1-10 .mu.M.

IT **229003-12-7P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(intermediate; prepn. of substituted heterocyclic ureas for treatment of cancerous cell growth mediated by **raf kinase**)

IT **229002-65-7P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(prepn. of substituted heterocyclic ureas for treatment of cancerous cell growth mediated by **raf kinase**)

IT **227623-30-5P 229002-62-4P 229002-63-5P 229002-66-8P 229002-67-9P 229002-70-4P 229002-72-6P 229002-74-8P 229002-75-9P 229002-76-0P 229002-93-1P 229002-95-3P 229002-96-4P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of substituted heterocyclic ureas for treatment of cancerous cell growth mediated by **raf kinase**)

IT **144378-33-6, Raf kinase**
RL: BPR (Biological process); BSU (Biological study, unclassified); MSC (Miscellaneous); BIOL (Biological study); PROC (Process)
(prepn. of substituted heterocyclic ureas for treatment of cancerous cell growth mediated by **raf kinase**)

IT **229003-21-8**
RL: RCT (Reactant); RACT (Reactant or reagent)
(reactant; prepn. of substituted heterocyclic ureas for treatment of cancerous cell growth mediated by **raf kinase**)

RE.CNT 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L45 ANSWER 3 OF 5 HCAPLUS COPYRIGHT 2002 ACS

AN 1999:421660 HCAPLUS
DN 131:44811
TI Preparation of aryl- and heteroaryl-substituted heterocyclic ureas as **raf kinase** inhibitors
IN **Dumas, Jacques; Khire, Uday; Lowinger, Timothy Bruno**; Paulsen, Holger; **Riedl, Bernd; Scott, William J.; Smith, Roger A.; Wood, Jill E.**; Hatoum-Mokdad, Holia; Johnson, Jeffrey; Redman, Aniko; Sibley, Robert
PA **Bayer** Corporation, USA
SO PCT Int. Appl., 58 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
PI	WO 9932455	A1	19990701	WO 1998-US26082	19981222	<--
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM					
	RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG					
	CA 2315713	AA	19990701	CA 1998-2315713	19981222	<--
	AU 9919055	A1	19990712	AU 1999-19055	19981222	<--
	EP 1056725	A1	20001206	EP 1998-963810	19981222	<--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO					
	BR 9814361	A	20011127	BR 1998-14361	19981222	<--
	JP 2001526269	T2	20011218	JP 2000-525392	19981222	<--
	NO 2000003231	A	20000822	NO 2000-3231	20000621	<--
PRAI	US 1997-996181	A	19971222	<--		
	WO 1998-US26082	W	19981222			

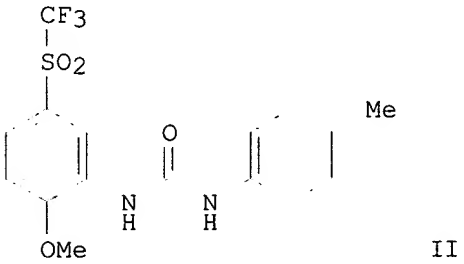
OS MARPAT 131:44811
AB The title compds. ANHCONHB (A = heteroaryl; B = aryl, heteroaryl), **raf kinase** inhibitors, were prepd. E.g., N-(1-phenyl-3-tert-butyl-5-pyrazolyl)-N'-(4-(4-pyridinylmethyl)phenyl)urea was prepd.
IT **227623-25-8P 227623-30-5P 227623-31-6P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of aryl- and heteroaryl-substituted heterocyclic ureas as **raf kinase** inhibitors)
IT **144378-33-6, Raf kinase**
RL: BSU (Biological study, unclassified); MSC (Miscellaneous); BIOL (Biological study)
(prepn. of aryl- and heteroaryl-substituted heterocyclic ureas as **raf kinase** inhibitors)
RE.CNT 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L45 ANSWER 4 OF 5 HCAPLUS COPYRIGHT 2002 ACS
AN 1999:421642 HCAPLUS
DN 131:58658
TI Inhibition of **raf kinase** using symmetrical and unsymmetrical substituted diphenyl ureas
IN **Miller, Scott; Osterhout, Martin; Dumas, Jacques; Khire, Uday; Lowinger, Timothy Bruno; Riedl, Bernd; Scott, William J.; Smith, Roger A.; Wood, Jill E.; Gunn, David; Rodriguez,**

Mareli; Wang, Ming
PA **Bayer** Corporation, USA
SO PCT Int. Appl., 89 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9932436	A1	19990701	WO 1998-US26081	19981222 <--
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	CA 2315646	AA	19990701	CA 1998-2315646	19981222 <--
	AU 9919054	A1	19990712	AU 1999-19054	19981222 <--
	EP 1049664	A1	20001108	EP 1998-963809	19981222 <--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	JP 2001526258	T2	20011218	JP 2000-525373	19981222 <--
	NO 2000003230	A	20000821	NO 2000-3230	20000621 <--
PRAI	US 1997-996344	A	19971222 <--		
	WO 1998-US26081	W	19981222		

OS MARPAT 131:58658
GI



II

AB The invention relates to the use of a group of aryl ureas ANHCONHB [I; A = certain (un)substituted Ph, pyridinyl, or thien-2-yl groups; B = certain (un)substituted mono- to tricyclic aryl or heteroaryl groups] in treating raf-mediated diseases, and pharmaceutical compns. for use in such therapy. A subset of I are novel and are claimed per se. Approx. 160 invention compds. and numerous intermediates were prepd. For instance, reaction of tolyl isocyanate with 2-methoxy-5-(trifluoromethanesulfonyl)aniline in EtOAc gave title compd. II. In an in vitro **raf kinase** assay, all compds. displayed IC50 values between 1 nM and 10 .mu.M.

IT **370-50-3P 228399-32-4P 228399-33-5P**
228399-34-6P 228399-35-7P 228399-36-8P
228399-38-0P 228399-39-1P 228399-40-4P
228399-41-5P 228399-42-6P 228399-43-7P
228399-44-8P 228399-45-9P 228399-47-1P
228399-48-2P 228399-49-3P 228399-51-7P
228399-52-8P 228399-54-0P 228399-56-2P
228399-57-3P 228399-58-4P 228399-59-5P
228399-60-8P 228399-61-9P 228399-62-0P
228399-63-1P 228399-65-3P 228399-66-4P
228399-67-5P 228399-68-6P 228399-69-7P

228399-70-0P 228399-71-1P 228399-72-2P
228399-74-4P 228399-75-5P 228399-76-6P
228399-77-7P 228399-78-8P 228399-79-9P
228399-80-2P 228399-82-4P 228399-83-5P
228399-84-6P 228399-85-7P 228399-86-8P
228399-87-9P 228399-88-0P 228399-89-1P
228399-90-4P 228399-92-6P 228399-93-7P
228399-94-8P 228399-95-9P 228399-96-0P
228399-97-1P 228399-98-2P 228399-99-3P
228400-01-9P 228400-02-0P 228400-03-1P
228400-04-2P 228400-05-3P 228400-06-4P
228400-07-5P 228400-08-6P 228400-10-0P
228400-11-1P 228400-12-2P 228400-13-3P
228400-14-4P 228400-15-5P 228400-16-6P
228400-17-7P 228400-18-8P 228400-20-2P
228400-21-3P 228400-22-4P 228400-23-5P
228400-24-6P 228400-25-7P 228400-26-8P
228400-27-9P 228400-28-0P 228400-30-4P
228400-31-5P 228400-32-6P 228400-33-7P
228400-34-8P 228400-35-9P 228400-36-0P
228400-37-1P 228400-38-2P 228400-39-3P
228400-40-6P 228400-41-7P 228400-42-8P
228400-43-9P 228400-44-0P 228400-45-1P
228400-46-2P 228400-47-3P 228400-48-4P
228400-49-5P 228400-50-8P 228400-51-9P
228400-52-0P 228400-53-1P 228400-54-2P
228400-55-3P 228400-56-4P 228400-57-5P
228400-58-6P 228400-60-0P 228400-61-1P
228400-62-2P 228400-63-3P 228400-64-4P
228400-65-5P 228400-66-6P 228400-67-7P
228400-69-9P 228400-70-2P 228400-71-3P
228400-72-4P 228400-73-5P 228400-74-6P
228400-75-7P 228400-76-8P 228400-77-9P
228400-78-0P 228400-79-1P 228400-80-4P
228400-81-5P 228400-82-6P 228400-83-7P
228400-84-8P 228400-85-9P 228400-87-1P
228400-89-3P 228400-91-7P 228400-92-8P
228400-93-9P 228400-94-0P 228400-95-1P
228400-96-2P 228400-97-3P 228400-99-5P
228401-00-1P 228401-01-2P 228401-02-3P
228401-03-4P 228401-04-5P 228401-07-8P
228401-49-8P 228401-50-1P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of sym. and unsym. substituted di-Ph ureas with inhibitory effects on tumors mediated by **raf kinase**)

IT **144378-33-6, Raf Kinase**
RL: BPR (Biological process); BSU (Biological study, unclassified); MSC (Miscellaneous); BIOL (Biological study); PROC (Process)
(prepn. of sym. and unsym. substituted di-Ph ureas with inhibitory effects on tumors mediated by **raf kinase**)

RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L45 ANSWER 5 OF 5 HCAPLUS COPYRIGHT 2002 ACS
AN 1998:776672 HCAPLUS
DN 130:38284
TI Preparation of urea derivatives as **raf kinase** inhibitors
IN **Wood, Jill E.**; Wild, Hanno; Rogers, Daniel H.; Lyons, John; Katz, Michael E.; Caringal, Yolanda V.; Dally, Robert; Lee, Wendy; **Smith, Roger A.**; Blum, Cheri L.

PA **Bayer** Corp., USA; Onyx Pharmaceuticals; et al.
SO PCT Int. Appl., 53 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9852559	A1	19981126	WO 1998-US10376	19980521 <--
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	AU 9875855	A1	19981211	AU 1998-75855	19980521 <--
	EP 986382	A1	20000322	EP 1998-923601	19980521 <--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
	JP 2002500650	T2	20020108	JP 1998-550618	19980521 <--
PRAI	US 1997-863021	A2	19970523 <--		
	WO 1998-US10376	W	19980521		

AB Substituted urea compds., useful for treating tumors mediated by **raf kinase** (no data), were prepd. E.g., reaction of Me thioglycolate and 3-chloro-4-methyl-2-pentenenitrile gave 16% of the 3-aminothiophene deriv., which was reacted with 4-MeC6H4NCO to give Me 5-isopropyl-3-(3-p-tolylureido)thiophene-2-carboxylate.

IT **216573-01-2P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(prepn. of urea derivs. as **raf kinase** inhibitors)

IT **216573-03-4P 216573-34-1P 216574-09-3P 216574-10-6P 216574-11-7P 216589-05-8P 216589-46-7P 216852-73-2P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of urea derivs. as **raf kinase** inhibitors)

IT **149719-32-4, v-Raf kinase**
RL: BSU (Biological study, unclassified); MSC (Miscellaneous); BIOL (Biological study)
(prepn. of urea derivs. as **raf kinase** inhibitors)

IT **216591-27-4P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of urea derivs. as **raf kinase** inhibitors)

RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d l46 bib abs hitrn tot

L46 ANSWER 1 OF 2 HCAPLUS COPYRIGHT 2002 ACS
AN 2001:746592 HCAPLUS
DN 136:95577
TI Discovery of heterocyclic ureas as a new class of **raf kinase** inhibitors: identification of a second generation lead by a combinatorial chemistry approach
AU **Smith, R. A.**; Barbosa, J.; Blum, C. L.; Bobko, M. A.; Caringal,

Y. V.; Dally, R.; Johnson, J. S.; Katz, M. E.; Kennure, N.; Kingery-Wood, J.; Lee, W.; **Lowinger, T. B.**; Lyons, J.; Marsh, V.; Rogers, D. H.; Swartz, S.; Walling, T.; Wild, H.

CS Department of Chemistry Research, **Bayer** Research Center, West Haven, CT, 06516, USA

SO Bioorganic & Medicinal Chemistry Letters (2001), 11(20), 2775-2778
CODEN: BMCLE8; ISSN: 0960-894X

PB Elsevier Science Ltd.

DT Journal

LA English

AB Heterocyclic ureas, such as N-3-thienyl N'-aryl ureas, have been identified as novel inhibitors of **raf kinase**, a key mediator in the ras signal transduction pathway. Structure-activity relationships were established, and the potency of the screening hit was improved 10-fold to IC50=1.7 .mu.M. A combinatorial synthesis approach enabled the identification of a breakthrough lead (IC50=0.54 .mu.M) for a second generation series of heterocyclic urea **raf kinase** inhibitors.

IT **144378-33-6, Raf kinase**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(heterocyclic ureas as **raf kinase** inhibitors)

IT **216572-95-1P 216573-01-2P 216573-03-4P**
216573-09-0P 216573-13-6P 216573-17-0P
216573-24-9P 216573-25-0P 216573-26-1P
216573-27-2P 216573-34-1P 216574-41-3P
216574-53-7P 216589-05-8P 216589-46-7P
216591-27-4P 229003-21-8P 329260-25-5P
329260-39-1P 329260-45-9P 329260-47-1P
329260-78-8P 329260-80-2P 329260-82-4P
329260-84-6P 371974-26-4P 389069-17-4P
389069-18-5P 389069-19-6P 389069-20-9P
389069-21-0P 389069-22-1P 389070-11-5P
389070-12-6P 389070-13-7P 389070-14-8P
389070-15-9P 389070-21-7P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(heterocyclic ureas as **raf kinase** inhibitors)

RE.CNT 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L46 ANSWER 2 OF 2 HCAPLUS COPYRIGHT 2002 ACS

AN 2000:493516 HCAPLUS

DN 133:120157

TI Preparation of .omega.-carboxy(hetero)aryl substituted diphenyl ureas as **raf kinase** inhibitors

IN **Riedl, Bernd; Dumas, Jacques; Khire, Uday; Lowinger, Timothy B.; Scott, William J.; Smith, Roger A.; Wood, Jill E.**; Monahan, Mary-Katherine; Natero, Reina; Renick, Joel; Sibley, Robert N.

PA **Bayer** Corporation, USA

SO PCT Int. Appl., 120 pp.
CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2000042012	A1	20000720	WO 2000-US648	20000112

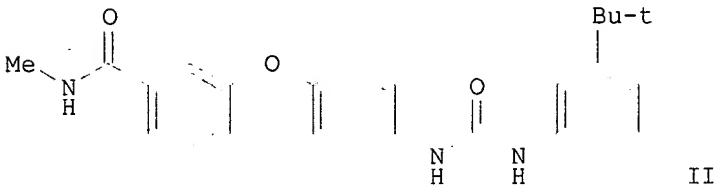
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI,

SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM,
AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE,
DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF,
CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

EP 1140840	A1	20011010	EP 2000-903239	20000112	
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO					
US 2001011135	A1	20010802	US 2001-773659	20010202	
US 2001011136	A1	20010802	US 2001-773675	20010202	
US 2001016659	A1	20010823	US 2001-773672	20010202	
US 2001027202	A1	20011004	US 2001-773658	20010202	
US 2001034447	A1	20011025	US 2001-773604	20010202	
NO 2001003463	A	20010912	NO 2001-3463	20010712	
US 2002042517	A1	20020411	US 2001-948915	20010910	
PRAI US 1999-115877P	P	19990113			
US 1999-257266	A2	19990225			
US 1999-425228	A2	19991022			
WO 2000-US648	W	20000112			

OS MARPAT 133:120157

GI



II

AB This invention relates to the prepn. and use of (hetero)aryl ureas ANHCONHB [I; A = L(ML1)q; L = 5- or 6-membered (hetero)aryl, esp. Ph or pyridinyl; M = bridging group; L1 = (hetero)aryl with at least one (un)substituted sulfamoyl, carboxy, or carbamoyl substituent; q = 1-3; B = certain (un)substituted mono- to tricyclic aryl or heteroaryl groups] for the treatment of raf mediated diseases, such as cancer (no data). Approx. 100 invention compds. and numerous intermediates were prepd. For instance, 3-tert-butylaniline was coupled with bis(trichloromethyl)carbonate to form the isocyanate, followed by addn. of 4-(3-N-methylcarbamoylphenoxy)aniline (prepn. given) to afford the urea II.

IT **284461-33-2P**, N-(3-tert-Butylphenyl)-N'-(4-(3-(N-methylcarbamoyl)phenoxy)phenyl)urea **284461-34-3P**, N-(3-tert-Butylphenyl)-N'-(4-(4-acetylphenoxy)phenyl)urea **284461-36-5P**, N-(5-tert-Butyl-2-methoxyphenyl)-N'-[4-[3-(N-methylcarbamoyl)phenoxy]phenyl]urea **284461-37-6P**, N-(5-tert-Butyl-2-methoxyphenyl)-N'-[4-[4-methoxy-3-(N-methylcarbamoyl)phenoxy]phenyl]urea **284461-39-8P**, N-(5-tert-Butyl-2-methoxyphenyl)-N'-[4-(1-oxoisoindolin-5-yloxy)phenyl]urea **284461-42-3P 284461-43-4P**, N-[2-Methoxy-5-(trifluoromethyl)phenyl]-N'-[3-(2-carbamoyl-4-pyridyloxy)phenyl]urea **284461-44-5P 284461-45-6P**, N-[2-Methoxy-5-(trifluoromethyl)phenyl]-N'-[4-(2-carbamoyl-4-pyridyloxy)phenyl]urea **284461-51-4P 284461-54-7P 284461-58-1P**, N-[2-Methoxy-5-(trifluoromethyl)phenyl]-N'-[4-[[2-(N-methylcarbamoyl)-4-pyridyl]thio]phenyl]urea **284461-74-1P**, N-[4-Chloro-3-(trifluoromethyl)phenyl]-N'-[4-(2-carbamoyl-4-pyridyloxy)phenyl]urea **284461-75-2P**, N-[4-Chloro-3-(trifluoromethyl)phenyl]-N'-[3-(2-carbamoyl-4-pyridyloxy)phenyl]urea **284461-78-5P 284461-86-5P 284461-90-1P**

284461-99-0P 284462-05-1P 284462-06-2P
284462-17-5P 284462-18-6P 284462-19-7P,
N-[4-Bromo-3-(trifluoromethyl)phenyl]-N'-[2-chloro-4-[[2-(N-methylcarbamoyl)-4-pyridyl]oxy]phenyl]urea **284462-20-0P,**
N-[4-Bromo-3-(trifluoromethyl)phenyl]-N'-[3-chloro-4-[[2-(N-methylcarbamoyl)-4-pyridyl]oxy]phenyl]urea **284462-22-2P,**
N-[4-Bromo-3-(trifluoromethyl)phenyl]-N'-[3-[[2-(N-methylcarbamoyl)-4-pyridyl]oxy]phenyl]urea **284462-26-6P 284462-28-8P,**
N-[2-Methoxy-4-chloro-5-(trifluoromethyl)phenyl]-N'-[4-[[2-(N-methylcarbamoyl)-4-pyridyl]oxy]phenyl]urea **284462-30-2P**
284462-31-3P, N-[2-Methoxy-4-chloro-5-(trifluoromethyl)phenyl]-N'-[3-[[2-(N-methylcarbamoyl)-4-pyridyl]oxy]phenyl]urea **284462-35-7P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(prepn. of .omega.-carboxy(hetero)aryl substituted di-Ph urea **raf kinase** inhibitors by reacting arylisocyanates with arylamines)

IT **228418-48-2P 284461-35-4P 284461-40-1P**
284461-41-2P 284461-46-7P 284461-47-8P
284461-49-0P 284461-50-3P 284461-52-5P
284461-53-6P 284461-55-8P 284461-56-9P
284461-57-0P 284461-59-2P 284461-60-5P
284461-61-6P 284461-62-7P 284461-63-8P
284461-64-9P 284461-65-0P 284461-66-1P
284461-67-2P 284461-68-3P 284461-69-4P
284461-70-7P 284461-71-8P 284461-72-9P
284461-77-4P 284461-79-6P 284461-80-9P
284461-81-0P 284461-82-1P 284461-83-2P
284461-84-3P 284461-85-4P 284461-88-7P
284461-91-2P 284461-92-3P 284461-93-4P
284461-94-5P 284461-95-6P 284461-96-7P
284461-97-8P 284461-98-9P 284462-00-6P
284462-01-7P 284462-02-8P 284462-03-9P
284462-04-0P 284462-07-3P 284462-08-4P
284462-09-5P 284462-10-8P 284462-11-9P
284462-12-0P 284462-13-1P 284462-15-3P
284462-16-4P 284462-21-1P 284462-23-3P
284462-24-4P 284462-25-5P 284462-27-7P
284462-32-4P 284462-33-5P 284462-34-6P
284462-36-8P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of .omega.-carboxy(hetero)aryl substituted di-Ph urea **raf kinase** inhibitors by reacting arylisocyanates with arylamines)

IT **284461-38-7,** N-(5-tert-Butyl-2-methoxyphenyl)-N'-[4-(1,3-dioxoisoindolin-5-yloxy)phenyl]urea **284461-48-9**
284461-76-3, N-[4-Chloro-3-(trifluoromethyl)phenyl]-N'-(3-((2-(N-Methylcarbamoyl)-4-pyridyl)oxy)phenyl)urea **284462-29-9**
284462-76-6 284671-00-7, N-[5-(Trifluoromethyl)-2-methoxyphenyl]-N'-[4-[3-(5-methoxycarbonylpyridyl)oxy]phenyl]urea
284671-01-8, N-[5-(Trifluoromethyl)-2-methoxyphenyl]-N'-(3-carboxyphenyl)urea
RL: RCT (Reactant); RACT (Reactant or reagent)
(prepn. of .omega.-carboxy(hetero)aryl substituted di-Ph urea **raf kinase** inhibitors by reacting arylisocyanates with arylamines)

IT **284461-73-0P 284461-89-8P 284462-67-5P,**
N-[4-Chloro-3-(trifluoromethyl)phenyl]-N'(4-aminophenyl)Urea
284462-68-6P, N-[4-Chloro-3-(trifluoromethyl)phenyl]-N'(4-

ethoxycarbonylphenyl)Urea **284462-69-7P 284462-70-0P**
284462-71-1P 284462-97-1P 284670-98-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of .omega.-carboxy(hetero)aryl substituted di-Ph urea **raf kinase** inhibitors by reacting arylisocyanates with arylamines)
RE.CNT 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> fil reg
FILE 'REGISTRY' ENTERED AT 11:16:56 ON 02 MAY 2002
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2002 American Chemical Society (ACS)

STRUCTURE FILE UPDATES: 30 APR 2002 HIGHEST RN 409303-45-3
DICTIONARY FILE UPDATES: 30 APR 2002 HIGHEST RN 409303-45-3

TSCA INFORMATION NOW CURRENT THROUGH July 7, 2001

Please note that search-term pricing does apply when conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Calculated physical property data is now available. See HELP PROPERTIES for more information. See STNote 27, Searching Properties in the CAS Registry File, for complete details:
http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf

=> d his l47-

(FILE 'HCAPLUS' ENTERED AT 11:04:15 ON 02 MAY 2002)

FILE 'REGISTRY' ENTERED AT 11:14:47 ON 02 MAY 2002

FILE 'HCAPLUS' ENTERED AT 11:15:08 ON 02 MAY 2002
SEL HIT RN L44

FILE 'REGISTRY' ENTERED AT 11:16:11 ON 02 MAY 2002
L47 332 S E1-E332
L48 2 S L47 AND L6,L12
L49 330 S L47 NOT L48

FILE 'REGISTRY' ENTERED AT 11:16:56 ON 02 MAY 2002

=> d ide can tot l48

L48 ANSWER 1 OF 2 REGISTRY COPYRIGHT 2002 ACS
RN **149719-32-4** REGISTRY
CN Kinase (phosphorylating), gene v-raf protein (9CI) (CA INDEX NAME)
OTHER NAMES:
CN **Gene v-raf kinase**
CN Gene v-raf serine-threonine protein kinase
CN **v-Raf kinase**
CN v-Raf serine/threonine kinase
MF Unspecified
CI MAN
SR CA
LC STN Files: BIOSIS, CA, CAPLUS, TOXCENTER

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
10 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
11 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 133:41379

REFERENCE 2: 130:38284

REFERENCE 3: 126:262519

REFERENCE 4: 126:142645

REFERENCE 5: 124:6073

REFERENCE 6: 122:6851

REFERENCE 7: 121:131197

REFERENCE 8: 119:244070

REFERENCE 9: 119:154375

REFERENCE 10: 119:153266

L48 ANSWER 2 OF 2 REGISTRY COPYRIGHT 2002 ACS
RN **144378-33-6** REGISTRY
CN Kinase (phosphorylating), gene c-raf protein (9CI) (CA INDEX NAME)
OTHER NAMES:
CN C-raf kinase
CN Gene c-Raf protein kinase
CN Gene raf serine/threonine kinase
CN Protein kinase c-Raf
CN Raf kinase
MF Unspecified
CI MAN
SR CA
LC STN Files: ADISNEWS, BIOBUSINESS, BIOSIS, CA, CAPLUS, CEN, CIN, PROMT, TOXCENTER, USPATFULL

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
294 REFERENCES IN FILE CA (1967 TO DATE)
5 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
297 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 136:279456

REFERENCE 2: 136:277868

REFERENCE 3: 136:277136

REFERENCE 4: 136:260900

REFERENCE 5: 136:260894

REFERENCE 6: 136:258141

REFERENCE 7: 136:226424

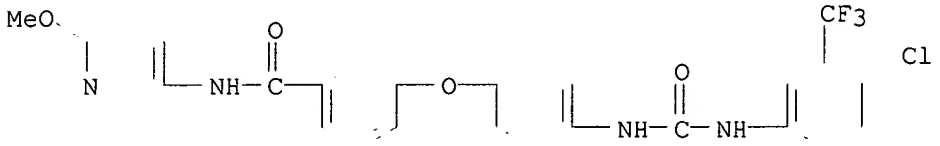
REFERENCE 8: 136:214136

REFERENCE 9: 136:213868

REFERENCE 10: 136:200113

=> d scan l49

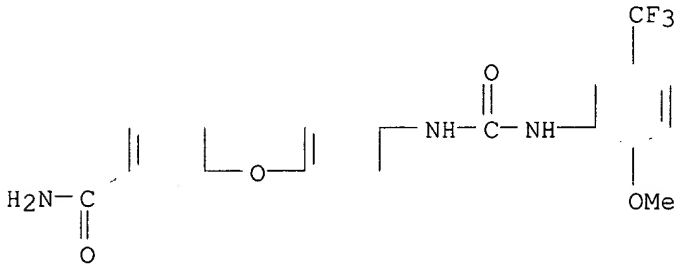
L49 330 ANSWERS REGISTRY COPYRIGHT 2002 ACS
IN Benzamide, 3-[4-[[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amin o]phenoxy]-N-(6-methoxy-3-pyridinyl)- (9CI)
MF C27 H20 Cl F3 N4 O4



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

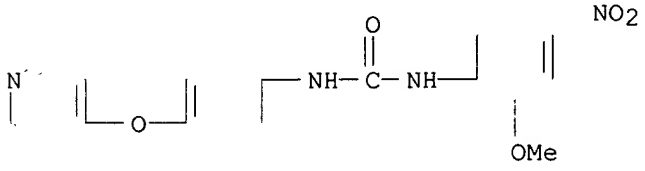
HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):25

L49 330 ANSWERS REGISTRY COPYRIGHT 2002 ACS
IN Benzamide, 3-[4-[[[[2-methoxy-5-(trifluoromethyl)phenyl]amino]carbonyl]ami no]phenoxy]- (9CI)
MF C22 H18 F3 N3 O4



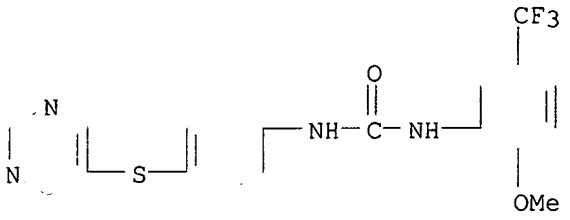
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L49 330 ANSWERS REGISTRY COPYRIGHT 2002 ACS
IN Urea, N-(2-methoxy-4-nitrophenyl)-N'-[4-(4-pyridinyloxy)phenyl]- (9CI)
MF C19 H16 N4 O5



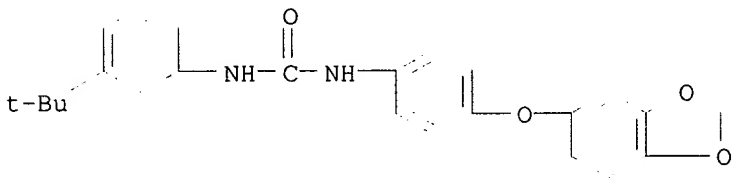
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L49 330 ANSWERS REGISTRY COPYRIGHT 2002 ACS
IN Urea, N-[2-methoxy-5-(trifluoromethyl)phenyl]-N'-[4-(5-pyrimidinylthio)phenyl]- (9CI)
MF C19 H15 F3 N4 O2 S



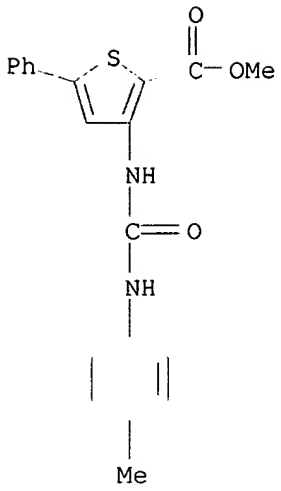
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L49 330 ANSWERS REGISTRY COPYRIGHT 2002 ACS
IN Urea, N-[4-(1,3-benzodioxol-5-yloxy)phenyl]-N'-[3-(1,1-dimethylethyl)phenyl]- (9CI)
MF C24 H24 N2 O4



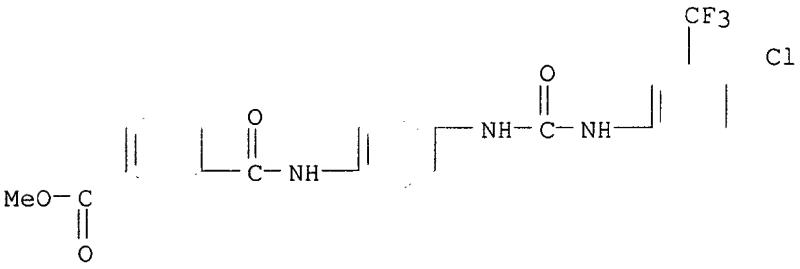
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L49 330 ANSWERS REGISTRY COPYRIGHT 2002 ACS
IN 2-Thiophenecarboxylic acid, 3-[[[(4-methylphenyl)amino]carbonyl]amino]-5-phenyl-, methyl ester (9CI)
MF C20 H18 N2 O3 S



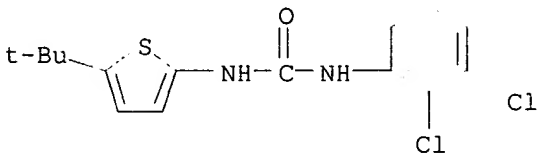
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L49 330 ANSWERS REGISTRY COPYRIGHT 2002 ACS
IN Benzoic acid, 3-[[[4-[[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenyl]amino]carbonyl]-, methyl ester (9CI)
MF C23 H17 Cl F3 N3 O4



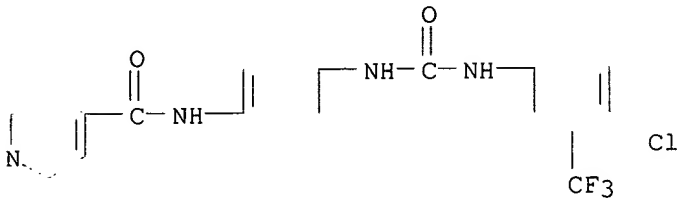
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L49 330 ANSWERS REGISTRY COPYRIGHT 2002 ACS
IN Urea, N-(2,3-dichlorophenyl)-N'-[5-(1,1-dimethylethyl)-2-thienyl]- (9CI)
MF C15 H16 Cl2 N2 O S



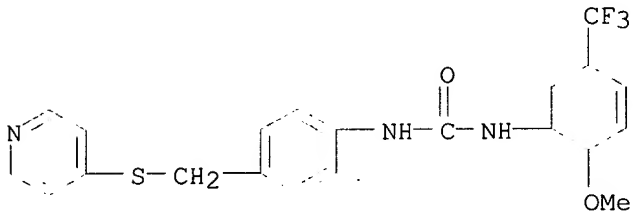
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L49 330 ANSWERS REGISTRY COPYRIGHT 2002 ACS
IN 4-Pyridinecarboxamide, N-[4-[[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenyl]- (9CI)
MF C20 H14 Cl F3 N4 O2



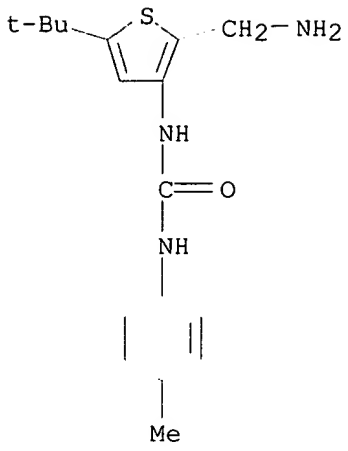
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L49 330 ANSWERS REGISTRY COPYRIGHT 2002 ACS
IN Urea, N-[2-methoxy-5-(trifluoromethyl)phenyl]-N'-[4-[(4-pyridinylthio)methyl]phenyl]- (9CI)
MF C21 H18 F3 N3 O2 S



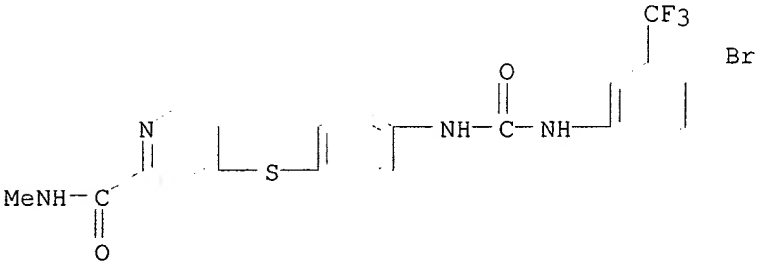
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L49 330 ANSWERS REGISTRY COPYRIGHT 2002 ACS
IN Urea, N-[2-(aminomethyl)-5-(1,1-dimethylethyl)-3-thienyl]-N'-(4-methylphenyl)- (9CI)
MF C17 H23 N3 O S



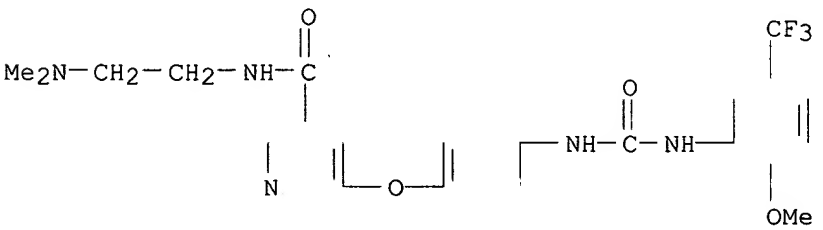
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L49 330 ANSWERS REGISTRY COPYRIGHT 2002 ACS
IN 2-Pyridinecarboxamide, 4-[[4-[[[[4-bromo-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenyl]thio]-N-methyl- (9CI)
MF C21 H16 Br F3 N4 O2 S



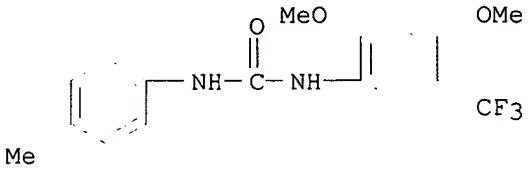
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L49 330 ANSWERS REGISTRY COPYRIGHT 2002 ACS
IN 3-Pyridinecarboxamide, N-[2-(dimethylamino)ethyl]-5-[4-[[[[2-methoxy-5-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]- (9CI)
MF C25 H26 F3 N5 O4



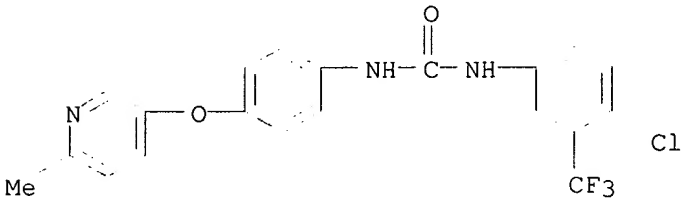
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L49 330 ANSWERS REGISTRY COPYRIGHT 2002 ACS
IN Urea, N-[2,4-dimethoxy-5-(trifluoromethyl)phenyl]-N'-(4-methylphenyl)-(9CI)
MF C17 H17 F3 N2 O3



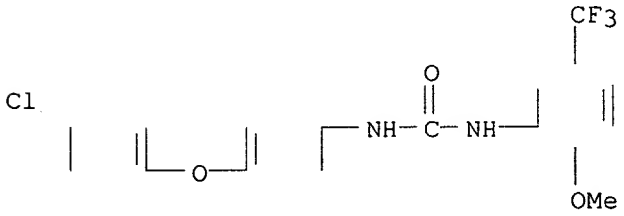
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L49 330 ANSWERS REGISTRY COPYRIGHT 2002 ACS
IN Urea, N-[4-chloro-3-(trifluoromethyl)phenyl]-N'-[4-[(6-methyl-3-pyridinyl)oxy]phenyl]- (9CI)
MF C20 H15 Cl F3 N3 O2



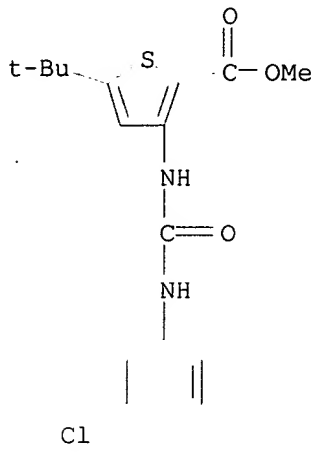
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L49 330 ANSWERS REGISTRY COPYRIGHT 2002 ACS
IN Urea, N-[4-(4-chlorophenoxy)phenyl]-N'-[2-methoxy-5-(trifluoromethyl)phenyl]- (9CI)
MF C21 H16 Cl F3 N2 O3



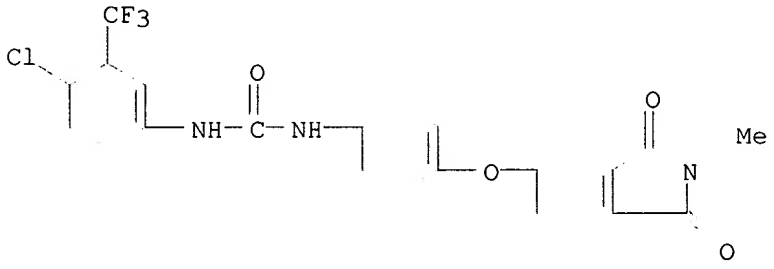
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L49 330 ANSWERS REGISTRY COPYRIGHT 2002 ACS
IN 2-Thiophenecarboxylic acid, 3-[[[(3-chlorophenyl)amino]carbonyl]amino]-5-(1,1-dimethylethyl)-, methyl ester (9CI)
MF C17 H19 Cl N2 O3 S



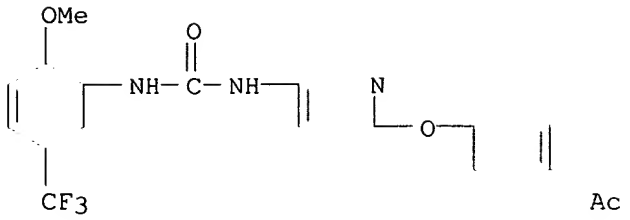
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L49 330 ANSWERS REGISTRY COPYRIGHT 2002 ACS
IN Urea, N-[4-chloro-3-(trifluoromethyl)phenyl]-N'-[4-[(2,3-dihydro-2-methyl-1,3-dioxo-1H-isoindol-5-yl)oxy]phenyl]- (9CI)
MF C23 H15 Cl F3 N3 O4



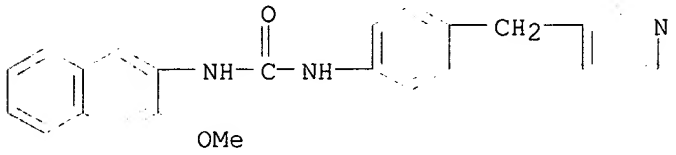
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L49 330 ANSWERS REGISTRY COPYRIGHT 2002 ACS
IN Urea, N-[6-(4-acetylphenoxy)-3-pyridinyl]-N'-[2-methoxy-5-(trifluoromethyl)phenyl]- (9CI)
MF C22 H18 F3 N3 O4



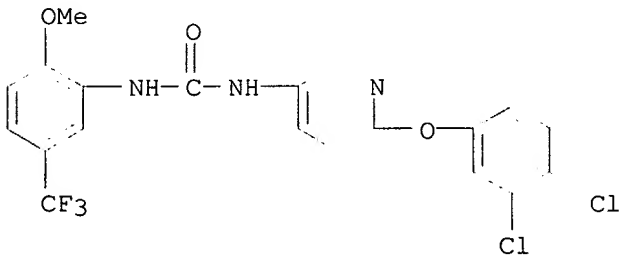
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L49 330 ANSWERS REGISTRY COPYRIGHT 2002 ACS
IN Urea, N-(3-methoxy-2-naphthalenyl)-N'-[4-(3-pyridinylmethyl)phenyl]- (9CI)
MF C24 H21 N3 O2



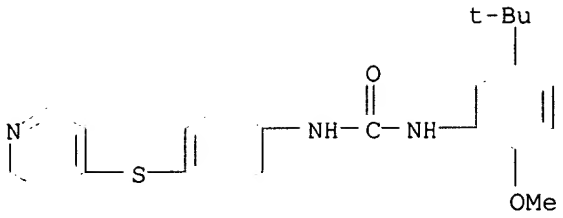
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L49 330 ANSWERS REGISTRY COPYRIGHT 2002 ACS
IN Urea, N-[6-(3,4-dichlorophenoxy)-3-pyridinyl]-N'-[2-methoxy-5-(trifluoromethyl)phenyl]- (9CI)
MF C20 H14 Cl2 F3 N3 O3



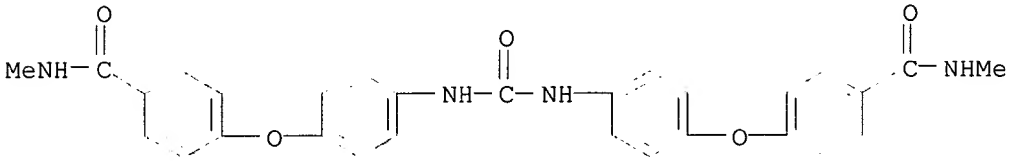
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L49 330 ANSWERS REGISTRY COPYRIGHT 2002 ACS
IN Urea, N-[5-(1,1-dimethylethyl)-2-methoxyphenyl]-N'-[4-(4-pyridinylthio)phenyl]- (9CI)
MF C23 H25 N3 O2 S



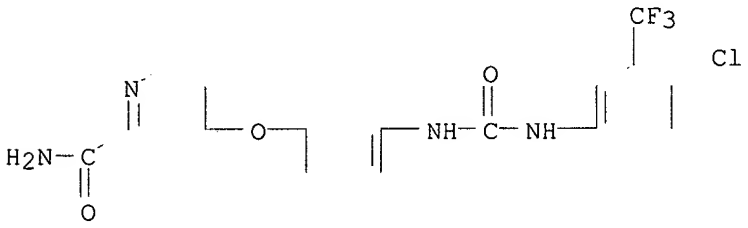
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L49 330 ANSWERS REGISTRY COPYRIGHT 2002 ACS
IN Benzamide, 4,4'-[carbonylbis(imino-4,1-phenyleneoxy)]bis[N-methyl- (9CI)
MF C29 H26 N4 O5



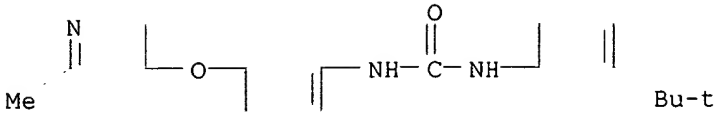
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L49 330 ANSWERS REGISTRY COPYRIGHT 2002 ACS
IN 2-Pyridinecarboxamide, 4-[3-[[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]- (9CI)
MF C20 H14 Cl F3 N4 O3



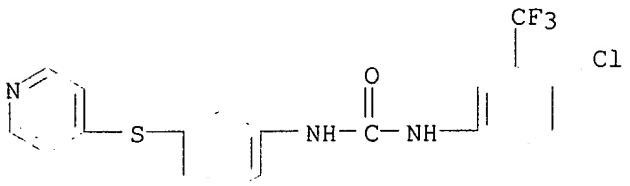
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L49 330 ANSWERS REGISTRY COPYRIGHT 2002 ACS
IN Urea, N-[3-(1,1-dimethylethyl)phenyl]-N'-[3-[(2-methyl-4-pyridinyl)oxy]phenyl]- (9CI)
MF C23 H25 N3 O2
CI COM



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L49 330 ANSWERS REGISTRY COPYRIGHT 2002 ACS
IN Urea, N-[4-chloro-3-(trifluoromethyl)phenyl]-N'-[3-(4-pyridinylthio)phenyl]- (9CI)
MF C19 H13 Cl F3 N3 O S



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):end

=> d his l50-

(FILE 'REGISTRY' ENTERED AT 11:16:56 ON 02 MAY 2002)
SAV L49 KUMAR776A/A
L50 23094 S L4 NOT L49

FILE 'HCAPLUS' ENTERED AT 11:17:55 ON 02 MAY 2002
L51 8301 S L50
L52 6940 S L16 AND L51
L53 1728 S L52 AND (1 OR 63)/SC,SX
E ANTITUMOR/CT
E E5+ALL
L54 303 S L52 AND E4,E3+NT

FILE 'HCAPLUS' ENTERED AT 11:38:35 ON 02 MAY 2002
L55 643 S L52 AND (?NEOPLAS? OR ?CANCER? OR ?CARCIN? OR ?TUMOR? OR ?TUM
L56 645 S L54,L55
L57 519 S L53 AND L56
L58 134 S L57 AND P/DT
L59 91 S L58 AND US/PC
L60 44 S L57 AND ?KINASE?
L61 19 S L60 AND L58
L62 1033 S L50 (L) THU/RL
L63 218 S L62 AND L57
L64 97 S L63 AND L58
L65 69 S L64 AND L59
L66 8 S L65 AND L60
L67 19 S L61,L66

=> fil hcaplus

FILE 'HCAPLUS' ENTERED AT 11:43:30 ON 02 MAY 2002
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

FILE COVERS 1907 - 2 May 2002 VOL 136 ISS 18
FILE LAST UPDATED: 30 Apr 2002 (20020430/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

CAS roles have been modified effective December 16, 2001. Please check your SDI profiles to see if they need to be revised. For information on CAS roles, enter HELP ROLES at an arrow prompt or use the CAS Roles thesaurus (/RL field) in this file.

=> d l67 bib abs hitrn fhitstr tot

L67 ANSWER 1 OF 19 HCAPLUS COPYRIGHT 2002 ACS
AN 2000:531658 HCAPLUS
DN 133:144896
TI Phosphonated agents and their antiangiogenic and **antitumorigenic** use
IN Collins, Delwood C.; Gagliardi, Antonio R.; Nickel, Peter
PA University of Kentucky Research Foundation, USA
SO U.S., 21 pp., Cont.-in-part of U.S. Ser. No. 899,996, abandoned.
CODEN: USXXAM
DT **Patent**
LA English
FAN.CNT 2

	PATENT NO.	KIND	DATE		APPLICATION NO.	DATE
PI	US 6096730	A	20000801		US 1998-121124	19980723 <--
	US 6160166	A	20001212		US 1999-357925	19990721 <--
PRAI	US 1997-899996	B2	19970724	<--		
	US 1998-121124	A3	19980723			

OS MARPAT 133:144896
AB Phosphonic acid agents are synthesized and characterized which are potent inhibitors of angiogenesis, **tumorigenesis** and metalloproteinase activity. Their method of use for the inhibition of angiogenesis and metalloproteinase and the treatment of **tumors** is also shown.
IT **145-63-1**, Suramin **220239-91-8**, NF 069
220239-92-9 220239-95-2, NF 068 **220239-96-3**,
NF 067
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(prepn. and pharmaceutical compn. of antiangiogenic and **antitumorigenic** phosphonic acid agents)
IT **111129-57-8P 220240-18-6P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and pharmaceutical compn. of antiangiogenic and

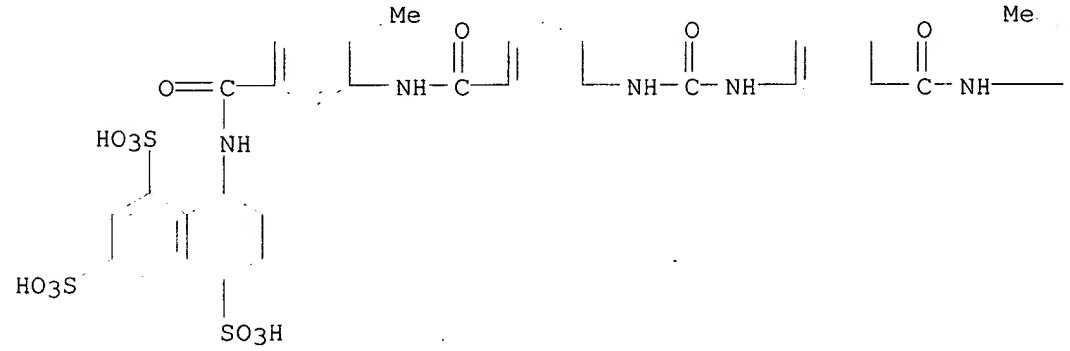
antitumorigenic phosphonic acid agents)

IT **145-63-1**, Suramin
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(prepn. and pharmaceutical compn. of antiangiogenic and **antitumorigenic** phosphonic acid agents)

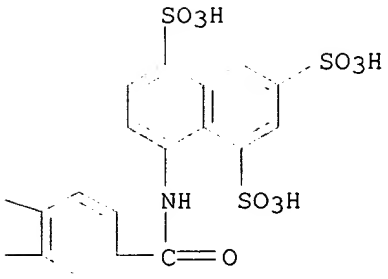
RN 145-63-1 HCAPLUS

CN 1,3,5-Naphthalenetrisulfonic acid, 8,8'-[carbonylbis[imino-3,1-phenylenecarbonylimino(4-methyl-3,1-phenylene)carbonylimino]]bis- (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 1-B



RE.CNT 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L67 ANSWER 2 OF 19 HCAPLUS COPYRIGHT 2002 ACS

AN 1999:425745 HCAPLUS

DN 131:87909

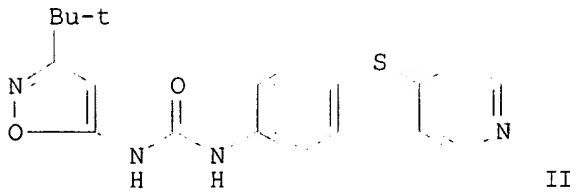
TI Inhibition of p38 **kinase** activity using substituted heterocyclic ureas

IN Dumas, Jacques; Khire, Uday; Lowinger, Timothy Bruno; Paulsen, Holger; Riedl, Bernd; Scott, William J.; Smith, Roger A.; Wood, Jill E.; Hatoum-Mokdad, Holia; Johnson, Jeffrey; Lee, Wendy; Redman, Aniko

PA Bayer Corporation, USA
SO PCT Int. Appl., 126 pp.
CODEN: PIXXD2
DT **Patent**
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
PI	WO 9932111	A1	19990701	WO 1998-US26080	19981222	<--
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM					
	RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG					
	CA 2315720	AA	19990701	CA 1998-2315720	19981222	<--
	AU 9919971	A1	19990712	AU 1999-19971	19981222	<--
	AU 739642	B2	20011018			
	EP 1041982	A1	20001011	EP 1998-964709	19981222	<--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO					
	JP 2001526223	T2	20011218	JP 2000-525102	19981222	<--
PRAI	US 1997-995750	A	19971222	<--		
	WO 1998-US26080	W	19981222			

OS MARPAT 131:87909
GI



II

AB A method for treatment of p38-mediated disease other than **cancer** comprises administration of ANHCONHB [I; A = substituted isoxazolyl, pyrazolyl, thienyl, furyl; B = (substituted) mono-, di-, or tricyclic aryl, heteroaryl contg. .gtoreq.1 5-6 membered arom. structure contg. 0-4 N, O, or S atoms]. Reaction of 4-(4-pyridinylthio)aniline with 3-tert-butyl-5-isoxazolyl isocyanate in toluene gave title compd. II. In an in vitro p38 **kinase** assay, I displayed IC50 values of 1-10 .mu.M.

IT **229003-12-7P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; prepn. of substituted heterocyclic ureas for treatment of p38 **kinase**-mediated diseases other than **cancer**)

IT **229002-65-7P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(prepn. of substituted heterocyclic ureas for treatment of p38 **kinase**-mediated diseases other than **cancer**)

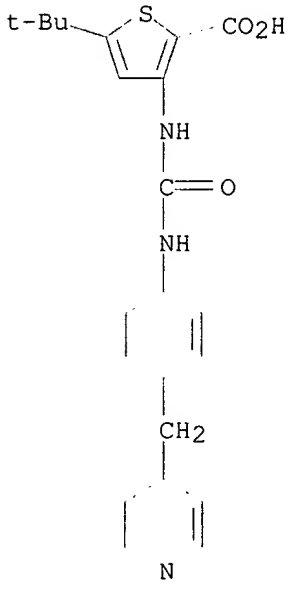
IT **227623-30-5P 227623-31-6P 229002-62-4P**
229002-63-5P 229002-66-8P 229002-67-9P
229002-70-4P 229002-72-6P 229002-74-8P

229002-76-0P 229002-93-1P 229002-95-3P
229002-96-4P 229155-57-1P 229155-58-2P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of substituted heterocyclic ureas for treatment of p38 **kinase**-mediated diseases other than **cancer**)

IT **229003-21-8**
RL: RCT (Reactant); RACT (Reactant or reagent)
(reactant; prepn. of substituted heterocyclic ureas for treatment of p38 **kinase**-mediated diseases other than **cancer**)

IT **229003-12-7P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; prepn. of substituted heterocyclic ureas for treatment of p38 **kinase**-mediated diseases other than **cancer**)

RN 229003-12-7 HCAPLUS
CN 2-Thiophenecarboxylic acid, 5-(1,1-dimethylethyl)-3-[[[[4-(4-pyridinylmethyl)phenyl]amino]carbonyl]amino]- (9CI) (CA INDEX NAME)



RE.CNT 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L67 ANSWER 3 OF 19 HCAPLUS COPYRIGHT 2002 ACS
AN 1999:421667 HCAPLUS
DN 131:58659
TI Preparation of diaryl ureas as inhibitors of p38 **kinase**.
IN Miller, Scott; Osterhout, Martin; Dumas, Jacques; Khire, Uday; Lowinger, Timothy Bruno; Riedl, Bernd; Scott, William J.; Smith, Roger A.; Wood, Jill E.; Gunn, David; Hatoum-Mokdad, Holia; Rodriguez, Mareli; Sibley, Robert; Wang, Ming
PA Bayer Corporation, USA
SO PCT Int. Appl., 107 pp.
CODEN: PIXXD2
DT **Patent**
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

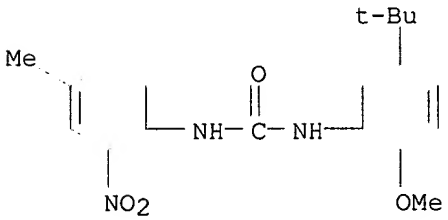
PI WO 9932463 A1 19990701 WO 1998-US27265 19981222 <--
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
CA 2315715 AA 19990701 CA 1998-2315715 19981222 <--
AU 9919399 A1 19990712 AU 1999-19399 19981222 <--
EP 1042305 A1 20001011 EP 1998-964221 19981222 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO
JP 2001526276 T2 20011218 JP 2000-525400 19981222 <--
PRAI US 1997-995749 A 19971222 <--
WO 1998-US27265 W 19981222
OS MARPAT 131:58659
AB A method of treating a p-38 mediated disease other than **cancer** comprises administration of BNHCONHA [A = (substituted) Ph, pyridyl, 2-thienyl; B = (substituted) aryl, heteroaryl contg. .gtoreq.1 6-membered arom. structure contg. 0-4 N, O, or S atoms]. Thus, 5-tert-butyl-2-(3-tetrahydrofuranyloxy)aniline (prepn. given) and p-tolyl isocyanate were stirred 8 h in PhMe to give 75% N-(5-tert-butyl-2-(3-tetrahydrofuranyloxy)phenyl)-N'-(4-methylphenyl)urea. Title compds. inhibited p38 **kinase** with IC50 = 1-10 .mu.M.
IT **228416-78-2P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(prepn. of diaryl ureas as inhibitors of p38 **kinase**)
IT **370-50-3P 117745-34-3P 228399-32-4P**
228399-33-5P 228399-34-6P 228399-35-7P
228399-38-0P 228399-44-8P 228399-45-9P
228399-61-9P 228399-62-0P 228399-63-1P
228399-65-3P 228399-66-4P 228399-68-6P
228399-69-7P 228399-70-0P 228399-71-1P
228399-72-2P 228399-74-4P 228399-82-4P
228399-84-6P 228400-63-3P 228400-64-4P
228400-65-5P 228400-87-1P 228400-92-8P
228400-93-9P 228400-94-0P 228400-95-1P
228400-96-2P 228400-97-3P 228400-99-5P
228401-00-1P 228401-01-2P 228401-02-3P
228401-03-4P 228401-04-5P 228401-07-8P
228416-61-3P 228416-62-4P 228416-63-5P
228416-64-6P 228416-65-7P 228416-66-8P
228416-67-9P 228416-68-0P 228416-69-1P
228416-70-4P 228416-71-5P 228416-72-6P
228416-73-7P 228416-74-8P 228416-75-9P
228416-76-0P 228416-79-3P 228416-81-7P
228416-83-9P 228416-85-1P 228416-87-3P
228416-89-5P 228416-91-9P 228416-93-1P
228416-96-4P 228416-99-7P 228417-03-6P
228417-06-9P 228417-09-2P 228417-12-7P
228417-14-9P 228417-18-3P 228417-21-8P
228417-24-1P 228417-27-4P 228417-30-9P
228417-33-2P 228417-36-5P 228417-38-7P
228417-40-1P 228417-42-3P 228417-44-5P
228417-46-7P 228417-48-9P 228417-50-3P
228417-52-5P 228417-53-6P 228417-54-7P
228417-55-8P 228417-56-9P 228417-57-0P
228417-58-1P 228417-59-2P 228417-60-5P

228417-61-6P 228417-62-7P 228417-63-8P
228417-64-9P 228417-65-0P 228417-66-1P
228417-67-2P 228417-68-3P 228417-69-4P
228417-70-7P 228417-71-8P 228417-72-9P
228417-74-1P 228417-76-3P 228417-78-5P
228417-79-6P 228417-80-9P 228417-81-0P
228417-82-1P 228417-83-2P 228417-84-3P
228417-85-4P 228417-86-5P 228417-87-6P
228417-88-7P 228417-89-8P 228417-90-1P
228417-91-2P 228417-92-3P 228417-93-4P
228417-94-5P 228417-95-6P 228417-96-7P
228417-97-8P 228417-98-9P 228417-99-0P
228418-00-6P 228418-01-7P 228418-02-8P
228418-03-9P 228418-04-0P 228418-05-1P
228418-06-2P 228418-07-3P 228418-08-4P
228418-09-5P 228418-11-9P 228418-12-0P
228418-13-1P 228418-14-2P 228418-15-3P
228418-16-4P 228418-17-5P 228418-18-6P
228418-19-7P 228418-20-0P 228418-21-1P
228418-23-3P 228418-24-4P 228418-25-5P
228418-26-6P 228418-27-7P 228418-28-8P
228418-31-3P 228418-32-4P 228418-33-5P
228418-36-8P 228418-37-9P 228418-38-0P
228418-39-1P 228418-40-4P 228418-41-5P
228418-42-6P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of diaryl ureas as inhibitors of p38 **kinase**)

IT **228399-41-5 228418-48-2 228418-49-3**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(prepn. of diaryl ureas as inhibitors of p38 **kinase**)

IT **228416-78-2P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(prepn. of diaryl ureas as inhibitors of p38 **kinase**)

RN 228416-78-2 HCAPLUS
CN Urea, N-[5-(1,1-dimethylethyl)-2-methoxyphenyl]-N'-(4-methyl-2-nitrophenyl)- (9CI) (CA INDEX NAME)



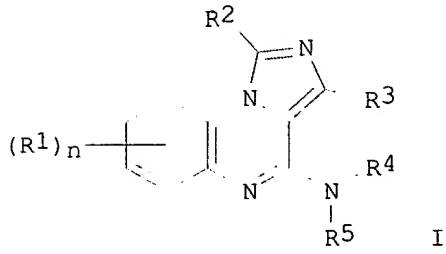
RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L67 ANSWER 4 OF 19 HCAPLUS COPYRIGHT 2002 ACS
AN 1999:166498 HCAPLUS
DN 130:223295
TI Preparation of imidazoquinoxaline protein tyrosine **kinase** inhibitors

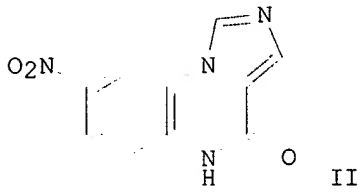
IN Barrish, Joel C.; Chen, Ping; Das, Jagabandhu; Iwanowicz, Edwin J.; Norris, Derek J.; Padmanabha, Ramesh; Roberge, Jacques Y.; Schieven, Gary L.
PA Bristol-Myers Squibb Company, USA
SO PCT Int. Appl., 315 pp.
CODEN: PIXXD2
DT **Patent**
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9909845	A1	19990304	WO 1998-US16027	19980803 <--
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6235740	B1	20010522	US 1998-97338	19980615 <--
AU 9886817	A1	19990316	AU 1998-86817	19980803 <--

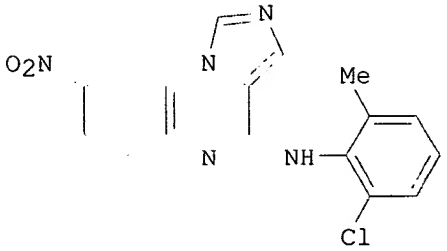
PRAI US 1997-56770P P 19970825 <--
US 1997-69159P P 19971209 <--
WO 1998-US16027 W 19980803
OS MARPAT 130:223295
GI



I



II



III

AB Novel imidazoquinoxalines I and salts thereof are disclosed [wherein: n = 0-4; R1, R2, R3 = H, R6, OH, OR6, SH, SR6, CO2H, SO3H, halo, cyano, NO2, etc.; R1-R3 may form ring(s); R4, R5 = H, R6, COR6; or NR4R5 forms (un)substituted 3- to 8-membered heterocyclic ring; R6 = (un)substituted alk(en/yn)yl, cycloalk(en)yl(alkyl), aryl, aralkyl, heterocyclo(alkyl)]. Also disclosed are pharmaceutical compns. contg. the compds., and methods of their use in the treatment of various protein tyrosine **kinase** -assocd. disorders, such as immunol. disorders (no data). Over 500 synthetic examples are given. For instance, the

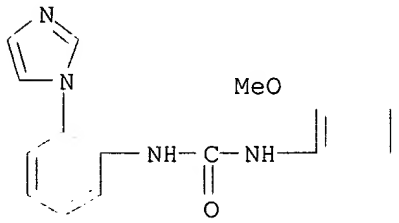
nitroimidazoloquinoxalinone II (prepd. in 4 steps) was treated with POCl3 to give 78% of the corresponding chloro compd., which reacted with NaN(SiMe3)2 and 2-chloro-6-methylaniline in THF to give 86% title compd. III.

IT **68008-32-2P 221068-10-6P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation) (intermediate; prepn. of imidazoquinoxalines as protein tyrosine **kinase** inhibitors)

IT **68008-32-2P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation) (intermediate; prepn. of imidazoquinoxalines as protein tyrosine **kinase** inhibitors)

RN 68008-32-2 HCAPLUS

CN Urea, N-[2-(1H-imidazol-1-yl)phenyl]-N'-(2-methoxyphenyl)- (9CI) (CA INDEX NAME)



RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L67 ANSWER 5 OF 19 HCAPLUS COPYRIGHT 2002 ACS

AN 1999:96248 HCAPLUS

DN 130:148689

TI Phosphonated agents and their antiangiogenic and **antitumorigenic** use

IN Collins, Delwood C.; Gagliardi, Antonio R.; Nickel, Peter

PA University of Kentucky Research Foundation, USA

SO PCT Int. Appl., 74 pp.
CODEN: PIXXD2

DT **Patent**

LA English

FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9905148	A1	19990204	WO 1998-US15470	19980724 <--
	W: AU, CA, JP, MX				
	RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	AU 9885915	A1	19990216	AU 1998-85915	19980724 <--
	AU 739637	B2	20011018		
	EP 1019419	A1	20000719	EP 1998-937133	19980724 <--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
PRAI	US 1997-899996	A	19970724 <--		
	WO 1998-US15470	W	19980724		

OS MARPAT 130:148689

AB The present invention relates to novel phosphonic acid substituted agents and their pharmaceutical compns. Phosphonic acid substituted agents that are potent inhibitors of angiogenesis or **tumorigenesis** is defined by the following formula: (P-Yn1)m1-Q1-K-(Q2-(Yn2-P)m2)j (P = phosphonic group, phosphonic salt; Y = OCO, NR1CO, CON(R1)R2; Q1, Q2 = aryl; K = H, NHCONH, NHCSNH, NHCOR3, NHCSR3CSNH; j, n1, n2 = 0-2; m1, m2 = 1-4; R1 = H, CH2CO2H, alkyl; R2 = alkyl, aryl, alkaryl; R3 = aryl). A

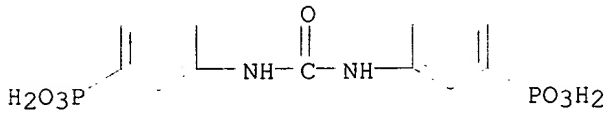
pharmaceutical compn. for the treatment of angiogenesis-dependent conditions or **tumors** comprises an effective amt. of a phosphonic acid agent and a pharmaceutically acceptable carrier. Some of the phosphonic acid agents were more potent inhibitors of angiogenesis in the chick chorioallantoic membrane (CAM) assay and to human microvascular endothelial cell growth than suramin.

IT **220240-08-4P 220240-09-5P 220240-14-2P**
220240-16-4P 220240-17-5P 220240-18-6P
RL: BAC (Biological activity or effector, except adverse); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(phosphonic acid agents and their antiangiogenic and **antitumorigenic** use)

IT **220239-81-6 220239-82-7 220239-83-8**
220239-84-9 220239-85-0 220239-86-1
220239-87-2 220239-88-3 220239-89-4
220239-90-7 220239-91-8 220239-92-9
220239-95-2 220239-96-3 220239-97-4
220239-98-5 220240-02-8 220240-03-9
RL: BAC (Biological activity or effector, except adverse); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(phosphonic acid agents and their antiangiogenic and **antitumorigenic** use)

IT **220240-08-4P**
RL: BAC (Biological activity or effector, except adverse); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(phosphonic acid agents and their antiangiogenic and **antitumorigenic** use)

RN 220240-08-4 HCAPLUS
CN Phosphonic acid, [carbonylbis(imino-3,1-phenylene)]bis- (9CI) (CA INDEX NAME)



RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L67 ANSWER 6 OF 19 HCAPLUS COPYRIGHT 2002 ACS
AN 1999:34888 HCAPLUS
DN 130:66491
TI Preparation of urea derivatives as inhibitors of p38
IN Salituro, Francesco Gerald; Bemis, Guy W.; Green, Jeremy; Kofron, James L.
PA Vertex Pharmaceuticals Incorporated, USA
SO PCT Int. Appl., 93 pp.
CODEN: PIXXD2
DT **Patent**
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9900357	A1	19990107	WO 1998-US13496	19980629 <--

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES,

FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG

US 6093742 A 20000725 US 1997-884160 19970627 <--
AU 9883776 A1 19990119 AU 1998-83776 19980629 <--
EP 993441 A1 20000419 EP 1998-934195 19980629 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI

PRAI US 1997-884160 A 19970627 <--
WO 1998-US13496 W 19980629

OS MARPAT 130:66491

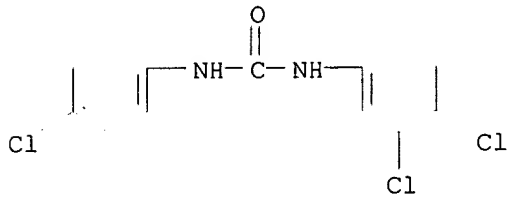
AB The title compds. WX1C(:Y)X2Z [W = (un)substituted satd., partially satd. or arom. monocyclic or bicyclic ring system optionally comprising up to 4 heteroatoms; Y = O, etc.; X1, X2 = O, S, etc.; Z = cycloalkyl, etc.] are prepd. Compds. of this invention are inhibitors of p38, a mammalian protein **kinase** involved in cell **proliferation**, cell death and response to extracellular stimuli. In in vitro assays for inhibition of phosphorylation of EGF receptor peptide, compds. of this invention showed IC50 values of 0.14 .mu.M to 19 .mu.M.

IT **101-20-2P 369-81-3P 1566-96-7P**
2008-73-3P 4300-43-0P 13114-79-9P
13141-95-2P 13142-35-3P 13142-47-7P
13142-48-8P 13142-50-2P 13143-23-2P
13208-22-5P 13256-73-0P 16655-20-2P
85260-98-6P 107917-67-9P 117745-34-3P
196617-12-6P 196617-13-7P 196700-19-3P
196700-39-7P 196700-55-7P 196700-64-8P
197800-69-4P 199741-56-5P 202598-90-1P
218134-88-4P 218134-90-8P 218134-91-9P
218134-92-0P 218134-93-1P 218134-94-2P
218134-95-3P 218134-96-4P 218134-97-5P
218134-98-6P 218134-99-7P 218135-01-4P
218135-02-5P 218135-03-6P 218135-04-7P
218135-05-8P 218135-06-9P 218135-07-0P
218135-08-1P 218135-10-5P 218135-11-6P
218135-12-7P 218135-13-8P 218135-14-9P
218135-15-0P 218135-16-1P 218135-19-4P
218135-20-7P 218135-21-8P 218135-22-9P
218135-23-0P 218135-24-1P 218135-26-3P
218135-27-4P 218135-28-5P 218135-29-6P
218135-30-9P 218135-32-1P 218135-33-2P
218135-34-3P 218135-35-4P 218135-36-5P
218135-37-6P 218135-38-7P 218135-40-1P
218135-41-2P 218135-42-3P 218135-43-4P
218135-44-5P 218135-45-6P 218135-47-8P
218135-48-9P 218135-49-0P 218135-50-3P
218135-51-4P 218135-53-6P 218135-54-7P
218135-55-8P 218135-56-9P 218135-57-0P
218135-58-1P 218135-59-2P 218135-60-5P
218135-61-6P 218135-62-7P 218135-63-8P
218135-64-9P 218135-65-0P 218135-66-1P
218135-68-3P 218135-70-7P 218135-72-9P
218135-74-1P 218135-78-5P 218135-80-9P
218135-83-2P 218135-86-5P 218135-90-1P
218135-94-5P 218135-96-7P 218135-99-0P
218136-00-6P 218136-01-7P 218136-02-8P
218136-03-9P 218136-04-0P 218136-05-1P
218136-06-2P 218136-07-3P 218136-08-4P
218136-09-5P 218136-10-8P 218136-11-9P
218136-12-0P 218136-13-1P 218136-14-2P
218136-15-3P 218136-17-5P 218136-18-6P
218136-19-7P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); **THU (Therapeutic**

use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of urea derivs. as inhibitors of p38)

IT **101-20-2P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of urea derivs. as inhibitors of p38)

RN 101-20-2 HCAPLUS
CN Urea, N-(4-chlorophenyl)-N'-(3,4-dichlorophenyl)- (9CI) (CA INDEX NAME)

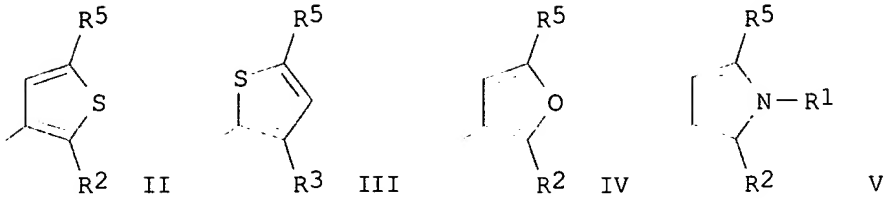


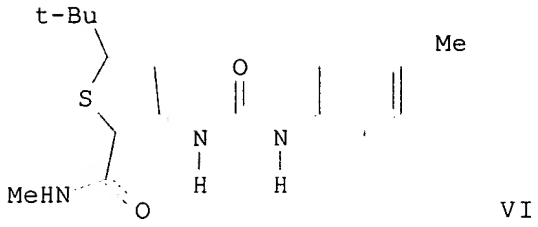
RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L67 ANSWER 7 OF 19 HCAPLUS COPYRIGHT 2002 ACS
AN 1998:776671 HCAPLUS
DN 130:38286
TI Inhibition of p38 **kinase** activity by aryl ureas
IN Ranges, Gerald; Scott, William; Bombara, Michael; Rauner, Deborah; Redman, Aniko; Smith, Roger; Paulsen, Holger; Chen, Jinshan; Gunn, David; Renick, Joel
PA Bayer Corp., USA; et al.
SO PCT Int. Appl., 84 pp.
CODEN: PIXXD2
DT **Patent**
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE		APPLICATION NO.	DATE	
PI	WO 9852558	A1	19981126		WO 1998-US10375	19980521	<--
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM						
	RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG						
	AU 9875854	A1	19981211		AU 1998-75854	19980521	<--
	EP 1019040	A1	20000719		EP 1998-923600	19980521	<--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI						
	JP 2001526687	T2	20011218		JP 1998-550617	19980521	<--
	US 6344476	B1	20020205		US 1998-83396	19980522	<--
PRAI	US 1997-863022	A2	19970523	<--			
	US 1997-98557P	P	19970523	<--			
	WO 1998-US10375	W	19980521				

OS MARPAT 130:38286
GI





AB The title ureas ANHC(O)NHB [I; A = (un)substituted C6-12 aryl, C5-12 heteroaryl; B = II-V; R1 = H, C1-4 alkyl; R2, R3 = halo, COOR1, CN, etc.; R5 = C3-5 alkyl], useful in treating cytokine mediated diseases other than **cancer** and proteolytic enzyme mediated diseases other than **cancer**, were prepd. Thus, reaction of N-methyl-3-amino-5-tert-butylthiophene-2-carboxamide (prepn. given) with 4-methylphenyl isocyanate in PhMe afforded 44% the title compd. VI. Compds. I are useful in treating diseases mediated by TNF.alpha., MMP-1, MMP-3, IL-1, IL-6, or IL-8 such as rheumatoid arthritis, osteoporosis, asthma, septic shock, inflammatory bowel disease, or the result of host-vs.-graft reactions. All exemplified compds. I showed p38 IC50s of 1 nM - 10 .mu.M.

IT **216573-01-2P 216574-43-5P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(inhibition of p38 **kinase** activity by aryl ureas)

IT **216572-93-9P 216572-95-1P 216572-97-3P**
216572-99-5P 216573-03-4P 216573-05-6P
216573-07-8P 216573-09-0P 216573-11-4P
216573-13-6P 216573-15-8P 216573-16-9P
216573-17-0P 216573-21-6P 216573-22-7P
216573-23-8P 216573-24-9P 216573-25-0P
216573-26-1P 216573-27-2P 216573-28-3P
216573-29-4P 216573-30-7P 216573-31-8P
216573-32-9P 216573-33-0P 216573-34-1P
216573-35-2P 216573-36-3P 216573-37-4P
216573-38-5P 216573-40-9P 216573-42-1P
216573-43-2P 216573-45-4P 216573-47-6P
216573-48-7P 216573-49-8P 216573-50-1P
216573-51-2P 216573-52-3P 216573-53-4P
216573-54-5P 216573-55-6P 216574-08-2P
216574-09-3P 216574-10-6P 216574-11-7P
216574-12-8P 216574-13-9P 216574-14-0P
216574-15-1P 216574-16-2P 216574-17-3P
216574-18-4P 216574-19-5P 216574-20-8P
216574-21-9P 216574-22-0P 216574-23-1P
216574-24-2P 216574-25-3P 216574-26-4P
216574-27-5P 216574-28-6P 216574-29-7P
216574-30-0P 216574-31-1P 216574-32-2P

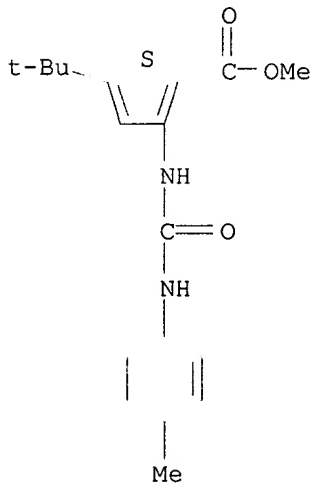
216574-33-3P 216574-34-4P 216574-35-5P
216574-36-6P 216574-37-7P 216574-38-8P
216574-39-9P 216574-40-2P 216574-41-3P
216574-42-4P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(inhibition of p38 **kinase** activity by aryl ureas)

IT **216574-76-4 216574-77-5**
RL: RCT (Reactant); RACT (Reactant or reagent)
(inhibition of p38 **kinase** activity by aryl ureas)

IT **216574-53-7P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(inhibition of p38 **kinase** activity by aryl ureas)

IT **216573-01-2P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); **THU (Therapeutic use)**; **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(inhibition of p38 **kinase** activity by aryl ureas)

RN 216573-01-2 HCAPLUS
CN 2-Thiophenecarboxylic acid, 5-(1,1-dimethylethyl)-3-[[[(4-methylphenyl)amino]carbonyl]amino]-, methyl ester (9CI) (CA INDEX NAME)



RE.CNT 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L67 ANSWER 8 OF 19 HCAPLUS COPYRIGHT 2002 ACS
AN 1998:352627 HCAPLUS
DN 129:54476
TI Protein **kinase** inhibitors for treatment of neurological disorders
IN Lewis, Michael E.; Kauer, James C.; Neff, Nicola; Roberts-Lewis, Jill; Murakata, Chikara; Saito, Hiromitsu; Matsuda, Yuzuru; Glicksman, Marcie A.; Kanai, Fumihiko; Kaneko, Masami
PA Cephalon, Inc., USA; Kyowa Hakko Kogyo Co., Ltd.
SO U.S., 61 pp. Cont.-in-part of U.S. Ser. No. 329,540.
CODEN: USXXAM
DT **Patent**
LA English
FAN.CNT 6

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

PI	US 5756494	A	19980526	US 1995-456642	19950602 <--
	US 5461146	A	19951024	US 1993-96561	19930722 <--
	EP 768312	A2	19970416	EP 1996-116661	19930726 <--
	EP 768312	A3	19970604		
	EP 768312	B1	20000906		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
	EP 1002534	A1	20000524	EP 1999-120008	19930726 <--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE				
	US 5621100	A	19970415	US 1994-329540	19941026 <--
	CA 2203767	AA	19960509	CA 1995-2203767	19951004 <--
	WO 9613506	A1	19960509	WO 1995-US12965	19951004 <--
	W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TT				
	RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	AU 9539516	A1	19960523	AU 1995-39516	19951004 <--
	AU 704314	B2	19990422		
	EP 788501	A1	19970813	EP 1995-937391	19951004 <--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
	BR 9509480	A	19970930	BR 1995-9480	19951004 <--
	JP 10510514	T2	19981013	JP 1995-514605	19951004 <--
	EP 1125938	A1	20010822	EP 2001-110483	19951004 <--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV				
	US 5741808	A	19980421	US 1997-800383	19970214 <--
PRAI	US 1992-920102	B2	19920724 <--		
	US 1993-96561	A2	19930722 <--		
	US 1994-329540	A2	19941026 <--		
	EP 1993-917337	A3	19930726 <--		
	EP 1996-116661	A3	19930726 <--		
	US 1995-456642	A	19950602 <--		
	EP 1995-937391	A3	19951004 <--		
	WO 1995-US12965	W	19951004 <--		

GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Derivs. of K-252a I (R = HO, MeO; R1 = H, Br, NHCONHPh, CH2SPh, 2-pyrimidinylthiomethyl, 2-furylmethylthiomethyl, etc.; R2 = H, Br, Cl, CH2OH, etc.; R 3 = CH2OH, CO2Me, CH2NHCO2Ph, CONHPh, CH2NHCO2Me, etc.; Z = O, H2), as well as novel bis-N-substituted derivs. of staurosporine XNMeWNMeX (W = C(:Y)NH, W1NHC(:Y); W1 = hydrocarbylene radical of 2-20 carbon atoms; Y = O, S) were prepd. The invention also features a method for treating diseased neuronal cells involving the administration of either the novel staurosporine derivs. or specified functional derivs. of K-252a. Thus, staurosporine was treated with hexamethyl-bis-isocyanate to give 1,6-hexamethylene-bis-(carbamylstaurosporine). The spinal cord choline acetyltransferase (CHAT) activity of I (R = OH, R1 = R2 = Br; R3 = CH2OH, Z = H2) at 300 nM was 146 compared with K-252a of 100.

IT **121664-76-4P**
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of staurosporine and K-252a derivs. as protein **kinase** inhibitors for treatment of neurol. disorders)

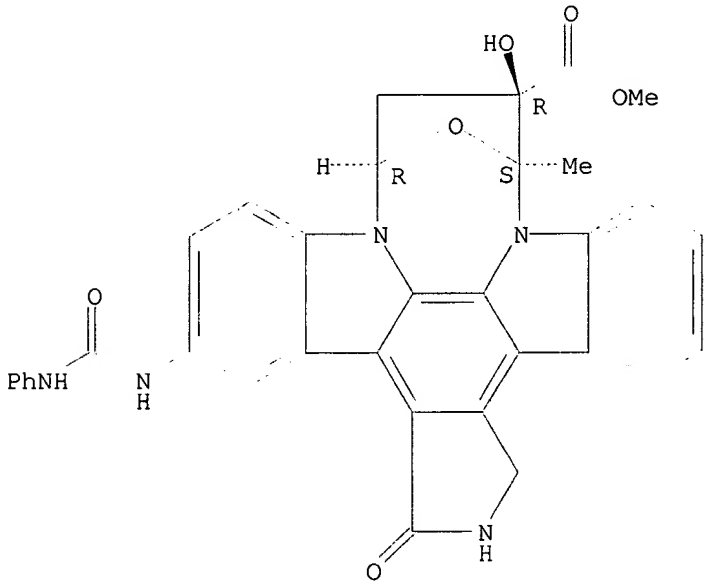
IT **121664-76-4P**

RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of staurosporine and K-252a derivs. as protein **kinase** inhibitors for treatment of neurol. disorders)

RN 121664-76-4 HCAPLUS

CN 9,12-Epoxy-1H-diindolo[1,2,3-fg:3',2',1'-kl]pyrrolo[3,4-i][1,6]benzodiazocine-10-carboxylic acid, 2,3,9,10,11,12-hexahydro-10-hydroxy-9-methyl-1-oxo-16-[[(phenylamino)carbonyl]amino]-, methyl ester, (9S,10R,12R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L67 ANSWER 9 OF 19 HCAPLUS COPYRIGHT 2002 ACS

AN 1998:202672 HCAPLUS

DN 128:257439

TI Preparation of 6-arylpyrido[2,3-d]pyrimidines and naphthyridines for inhibiting protein tyrosine **kinase** mediated cellular **proliferation**

IN Blankley, Clifton John; Doherty, Annette Marian; Hamby, James Marino; Panek, Robert Lee; Schroeder, Mel Conrad; Showalter, Howard Daniel Hollis; Connolly, Cleo

PA USA

SO U.S., 36 pp. Cont.-in-part of U.S. Ser. No. 339,051, abandoned.
CODEN: USXXAM

DT **Patent**

LA English

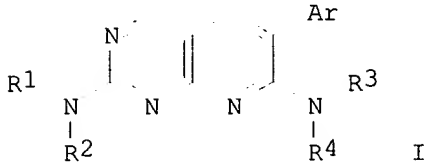
FAN.CNT 2

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 5733913	A	19980331	US 1995-539410	19951106 <--
CA 2199964	AA	19960523	CA 1995-2199964	19951113 <--
WO 9615128	A2	19960523	WO 1995-US14700	19951113 <--
W: AM, AU, BG, BY, CA, CN, CZ, EE, FI, GE, HU, JP, KG, KR, KZ, LT, LV, MD, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TJ, UA, UZ				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
AU 9641078	A1	19960606	AU 1996-41078	19951113 <--
AU 711426	B2	19991014		
EP 790997	A2	19970827	EP 1995-939129	19951113 <--

	EP 790997	B1	20000322			
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE					
	HU 76853	A2	19971229	HU 1997-1511	19951113	<--
	CN 1169726	A	19980107	CN 1995-196230	19951113	<--
	JP 10509452	T2	19980914	JP 1995-516240	19951113	<--
	CZ 286160	B6	20000112	CZ 1997-1390	19951113	<--
	AT 190978	E	20000415	AT 1995-939129	19951113	<--
	ES 2146782	T3	20000816	ES 1995-939129	19951113	<--
	SK 281724	B6	20010710	SK 1997-609	19951113	<--
	PL 181893	B1	20011031	PL 1995-320169	19951113	<--
	ZA 9509675	A	19960529	ZA 1995-9675	19951114	<--
	IL 115970	A1	19990620	IL 1995-115970	19951114	<--
	FI 9701953	A	19970512	FI 1997-1953	19970507	<--
	NO 9702198	A	19970513	NO 1997-2198	19970513	<--
	US 5952342	A	19990914	US 1998-40792	19980318	<--
PRAI	US 1994-339051	B2	19941114	<--		
	US 1995-539410	A	19951106	<--		
	WO 1995-US14700	W	19951113	<--		

OS MARPAT 128:257439

GI



I

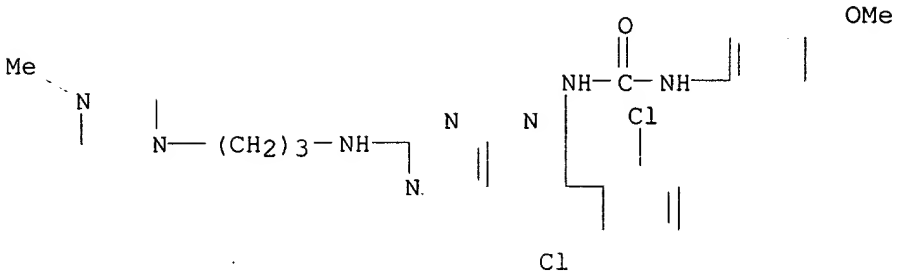
AB The title compds. [I; R1, R2, R4 = H, C1-8 alkyl, C2-8 alkenyl, etc.; R3 = C(O)R8, CO2R8, C(S)R8, etc.; R8 = H, C1-8 alkyl, C2-8 alkenyl, etc.; Ar = (un)substituted arom. ot heteroarom. selected from Ph, imidazolyl, pyrrolyl, etc.], inhibitors of protein tyrosine **kinase** which are esp. useful in treating atherosclerosis, restenosis, psoriasis, as well as bacterial infections, were prepd. and formulated. Thus, reaction of 2,7-diamino-6-(2,6-dichlorophenyl)pyrido[2,3-d]pyrimidine (prepn. described) with tert-Bu isocyanate in the presence of NaH in DMF afforded the urea I [R1 = R4 = H; R2 = R3 = C(O)NHtBu; Ar = 2,6-Cl2C6H3] which showed IC50 of 10.2 .mu.M against PDGF receptor tyrosine **kinase**.

IT **179342-64-4P 179342-65-5P 179342-66-6P**
179342-67-7P 179342-68-8P 179342-69-9P
179342-71-3P 179342-73-5P 179342-74-6P
179342-76-8P
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of 6-arylpyrido[2,3-d]pyrimidines and naphthyridines for inhibiting protein tyrosine **kinase** mediated cellular **proliferation**)

IT **179342-64-4P**
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of 6-arylpyrido[2,3-d]pyrimidines and naphthyridines for inhibiting protein tyrosine **kinase** mediated cellular **proliferation**)

RN 179342-64-4 HCAPLUS

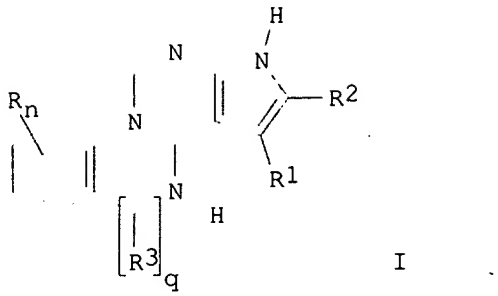
CN Urea, N-[6-(2,6-dichlorophenyl)-2-[[3-(4-methyl-1-piperazinyl)propyl]amino]pyrido[2,3-d]pyrimidin-7-yl]-N'-(4-methoxyphenyl)- (9CI) (CA INDEX NAME)



L67 ANSWER 10 OF 19 HCAPLUS COPYRIGHT 2002 ACS
AN 1998:147332 HCAPLUS
DN 128:192664
TI Preparation of substituted pyrrolopyrimidines as **antitumor** agents
IN Traxler, Peter; Bold, Guido; Lang, Marc; Frei, Jorg
PA Novartis A.-G., Switz.; Traxler, Peter; Bold, Guido; Lang, Marc; Frei, Jorg
SO PCT Int. Appl., 86 pp.
CODEN: PIXXD2
DT **Patent**
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
PI	WO 9807726	A1	19980226	WO 1997-EP4564	19970821	<--
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM					
	RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG					
	CN 1194647	A	19980930	CN 1996-196640	19960624	<--
	AU 9742064	A1	19980306	AU 1997-42064	19970821	<--
	AU 720429	B2	20000601			
	EP 938486	A1	19990901	EP 1997-940108	19970821	<--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI					
	JP 2000516626	T2	20001212	JP 1998-510425	19970821	<--
	US 6180636	B1	20010130	US 1999-242592	19990219	<--
PRAI	CH 1996-2071	A	19960823	<--		
	WO 1997-EP4564	A	19970821	<--		

OS MARPAT 128:192664
GI



I

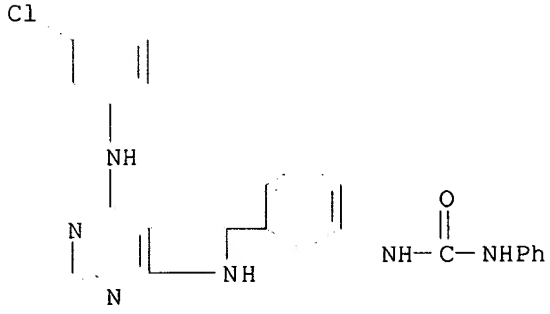
AB The title compds. [I; n = 0-3; q = 0-1; R = halo, lower alkyl, HOCH2, etc.; one of the radicals R1 and R2 = H, lower alkyl, and the other of the radicals R1 and R2 = (un)substituted Ph, amino-lower alkyl, piperidine-1-carbonyl, etc.], inhibitors of the tyrosine **kinase** activity of the receptor for the epidermal growth factor (EGF) and c-**erbB2kinase** and therefore useful as **antitumor** agents, were prepd. and formulated. Thus, hydrogenation of 4-(3-chloroanilino)-6-formyl-7H-pyrrolo[2,3-d]pyrimidine (prepn. described) with N-methylpiperazine in the presence of Raney Ni in DMPU, AcOH and MeOH afforded I [R = 3-Cl; R1 = H; R2 = 4-methylpiperazin-1-ylmethyl; q = 0]. Compds. I inhibit EGF-R-PTK activity by 50% (IC50), for example in a concn. of 0.0005-1 .mu.M, esp. from 0.001-1 .mu.M. Compds. I are effective at 0.5-2 g/day when administered to a patient of a body wt. of about 70 kg.

IT **203724-16-7P**
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of substituted pyrrolopyrimidines as **antitumor** agents)

IT **203724-16-7P**
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of substituted pyrrolopyrimidines as **antitumor** agents)

RN 203724-16-7 HCAPLUS

CN Urea, N-[3-[4-[(3-chlorophenyl)amino]-1H-pyrrolo[2,3-d]pyrimidin-6-yl]phenyl]-N'-phenyl- (9CI) (CA INDEX NAME)



L67 ANSWER 11 OF 19 HCAPLUS COPYRIGHT 2002 ACS

AN 1997:803799 HCAPLUS

DN 128:66489

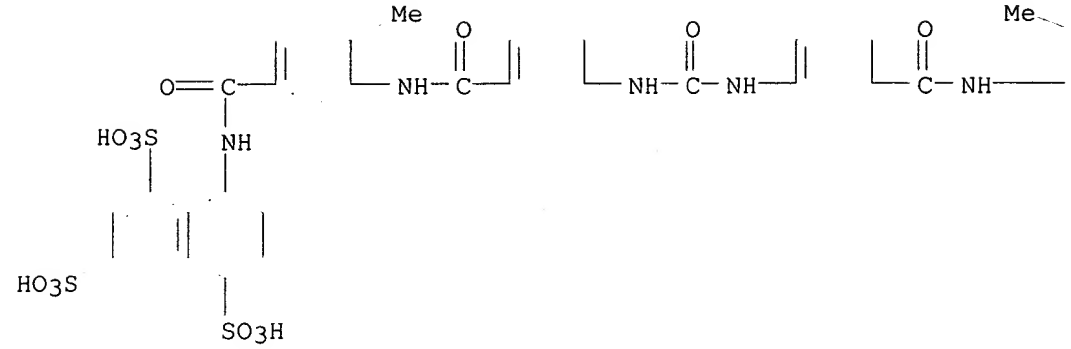
TI Compositions and methods for treating or preventing diseases of body

passageways
IN Hunter, William L.; Machan, Lindsay S.
PA Angiotech Pharmaceuticals, Inc., Can.; University of British Columbia; Hunter, William L.; Machan, Lindsay S.
SO PCT Int. Appl., 207 pp.
CODEN: PIXXD2
DT **Patent**
LA English
FAN.CNT 1

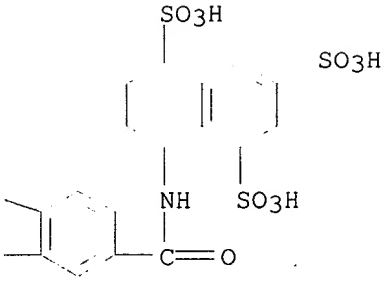
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9745105	A1	19971204	WO 1997-CA345	19970526 <--
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9727604	A1	19980105	AU 1997-27604	19970526 <--
AU 737078	B2	20010809		
EP 914102	A1	19990512	EP 1997-921563	19970526 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
CN 1219872	A	19990616	CN 1997-194908	19970526 <--
BR 9710682	A	19990817	BR 1997-10682	19970526 <--
JP 2000511161	T2	20000829	JP 1997-541313	19970526 <--
NO 9805463	A	19990121	NO 1998-5463	19981123 <--
KR 2000015944	A	20000315	KR 1998-709500	19981124 <--
PRAI US 1996-653207	A	19960524 <--		
WO 1997-CA345	W	19970526 <--		

AB The present invention provides methods for treating or preventing diseases assocd. with body passageways, comprising the step of delivering to an external portion of the body passageway a therapeutic agent. Representative examples of therapeutic agents include anti-angiogenic factors, anti-**proliferative** agents, anti-inflammatory agents, and antibiotics. Pastes and nanosprays contg. polycaprolactone were prepd.
IT **145-63-1**, Suramin
RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(compns. for treating or preventing diseases of body passageways)
IT **145-63-1**, Suramin
RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(compns. for treating or preventing diseases of body passageways)
RN 145-63-1 HCAPLUS
CN 1,3,5-Naphthalenetrisulfonic acid, 8,8'-[carbonylbis[imino-3,1-phenylenecarbonylimino(4-methyl-3,1-phenylene)carbonylimino]]bis- (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 1-B



L67 ANSWER 12 OF 19 HCAPLUS COPYRIGHT 2002 ACS
AN 1997:740435 HCAPLUS
DN 128:39550
TI Combinations of angiostatic compounds
IN Doshi, Rupa; Clark, Abbot F.
PA Clark, Abbot F., USA; Doshi, Rupa; Alcon Laboratories, Inc.
SO PCT Int. Appl., 52 pp.
CODEN: PIXXD2
DT **Patent**
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9741844	A1	19971113	WO 1997-US5574	19970403 <--
	W: AU, CA, JP, US				
	RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	AU 9724382	A1	19971126	AU 1997-24382	19970403 <--
PRAI	US 1996-17096P	P	19960509 <--		
	WO 1997-US5574	W	19970403 <--		

OS MARPAT 128:39550
AB The present invention is directed to compns. contg. combinations of

angiostatic compds. (chromans or benzofurans and e.g., steroids) and methods for their use in preventing pathol. neovascularization. Thus, 2-(5-hydroxy-2,4,6,7-tetramethyl-3,4-dihydrobenzo[1,2-b]furan-2-yl)ethyl 2-(6-methoxy-2-naphthyl)propionate (I) was prepd. by the reaction of 2-(5-hydroxy-2,4,6,7-tetramethyl-3,4-dihydrobenzo[1,2-b]furan-2-yl)ethanol with 6-methoxy-.alpha.-methylnaphthaleneacetic acid in the presence of dimethylaminopyridine and 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide-HCl in THF. Thus, a topical ocular soln. contained I 1.0, another angiostatic compd.0.005-5.0%, benzalkonium chloride 0.01, HPMC 0.5, NaCl 0.8, Na phosphate 0.28, and disodium edetate 0.01%, NaOH/HCl qs pH 7.2, and water qs to 100 mL.

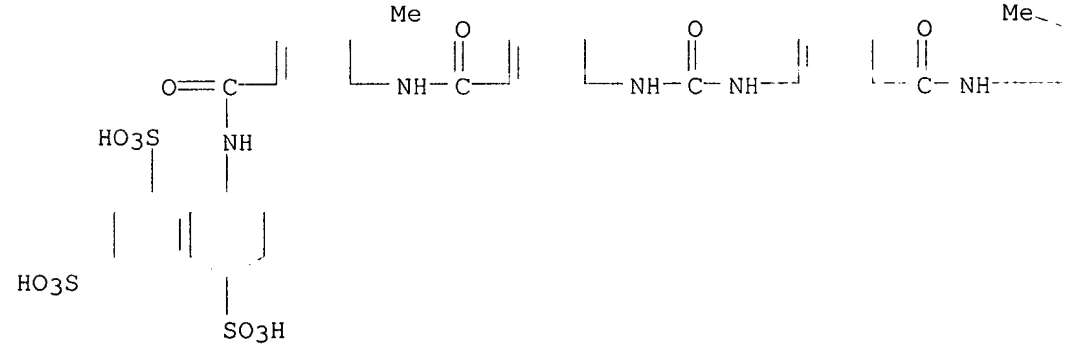
IT **145-63-1D**, Suramin, analogs
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmaceuticals contg. combinations of angiostatic compds.)

IT **145-63-1D**, Suramin, analogs
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmaceuticals contg. combinations of angiostatic compds.)

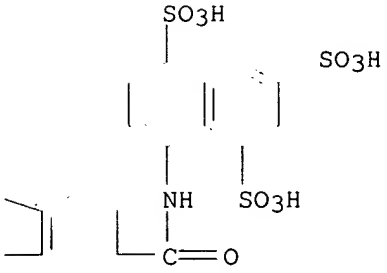
RN 145-63-1 HCAPLUS

CN 1,3,5-Naphthalenetrisulfonic acid, 8,8'-[carbonylbis[imino-3,1-phenylenecarbonylimino(4-methyl-3,1-phenylene)carbonylimino]]bis- (9CI) (CA INDEX NAME)

PAGE 1-A



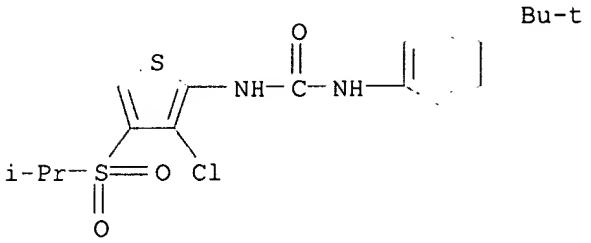
PAGE 1-B



L67 ANSWER 13 OF 19 HCAPLUS COPYRIGHT 2002 ACS
AN 1997:140236 HCAPLUS
DN 126:139899
TI Urea- and thiourea-type compounds capable of modulating tyrosine signal transduction
IN Tang, Peng Cho; McMahon, Gerald
PA Sugen, Inc., USA
SO PCT Int. Appl., 94 pp.
CODEN: PIXXD2
DT **Patent**
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9640673	A1	19961219	WO 1996-US9077	19960604 <--
	W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG				
	RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN				
	US 5773459	A	19980630	US 1995-486816	19950607 <--
	AU 9660493	A1	19961230	AU 1996-60493	19960604 <--
	JP 10175863	A2	19980630	JP 1996-359496	19961213 <--
PRAI	US 1995-486816		19950607 <--		
	WO 1996-US9077		19960604 <--		

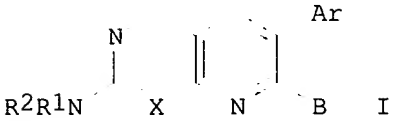
OS MARPAT 126:139899
AB The present invention relates to mols. capable of modulating tyrosine signal transduction to prevent and treat cell **proliferative** disorders or cell differentiation disorders assocd. with particular tyrosine **kinases** by inhibiting one or more abnormal tyrosine **kinase** activities. Four such compds. are N-[chloro-4-(isopropylsulfonyl)thien-2-yl]-N'-(4-t-butylphenyl)urea, N-[3-chloro-4-(isopropylsulfonyl)thien-2-yl]-N'-(3,5-ditrifluoromethylphenyl)urea, N-[2-(2,4-dichlorophenoxy)pyrid-5-yl]-N'-[4-trifluoromethyl(mercapto)phenyl]urea, and N-(4-cyanophenyl)-N'-[4-[(piperid-1-yl)sulfonyl]phenyl]thiourea. Disorders of Her2, EGFR, IGFR, PDGFR, met, Src and KDR/Flk-1 can be treated.
IT **186645-70-5P 186645-71-6P 186645-72-7P**
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of urea- and thiourea-type compds. capable of modulating tyrosine signal transduction)
IT **186645-70-5P**
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of urea- and thiourea-type compds. capable of modulating tyrosine signal transduction)
RN 186645-70-5 HCAPLUS
CN Urea, N-[3-chloro-4-[(1-methylethyl)sulfonyl]-2-thienyl]-N'-[4-(1,1-dimethylethyl)phenyl]- (9CI) (CA INDEX NAME)



L67 ANSWER 14 OF 19 HCAPLUS COPYRIGHT 2002 ACS
AN 1996:467130 HCAPLUS
DN 125:114688
TI Preparation of 6-aryl pyrido[2,3-d]pyrimidines and naphthyridines for inhibiting protein tyrosine **kinase**-mediated cellular **proliferation**
IN Blankley, Clifton John; Doherty, Annette Marian; Hamby, James Marino; Panek, Robert Lee; Schroeder, Mel Conrad; Showalter, Howard Daniel Hollis; Connolly, Cleo
PA Warner-Lambert Company, USA
SO PCT Int. Appl., 134 pp.
CODEN: PIXXD2
DT **Patent**
LA English
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
PI	WO 9615128	A2	19960523	WO 1995-US14700	19951113	<--
	W: AM, AU, BG, BY, CA, CN, CZ, EE, FI, GE, HU, JP, KG, KR, KZ, LT, LV, MD, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TJ, UA, UZ					
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE					
	US 5733913	A	19980331	US 1995-539410	19951106	<--
	AU 9641078	A1	19960606	AU 1996-41078	19951113	<--
	AU 711426	B2	19991014			
	EP 790997	A2	19970827	EP 1995-939129	19951113	<--
	EP 790997	B1	20000322			
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE					
	JP 10509452	T2	19980914	JP 1995-516240	19951113	<--
	AT 190978	E	20000415	AT 1995-939129	19951113	<--
	SK 281724	B6	20010710	SK 1997-609	19951113	<--
	PL 181893	B1	20011031	PL 1995-320169	19951113	<--
	FI 9701953	A	19970512	FI 1997-1953	19970507	<--
	NO 9702198	A	19970513	NO 1997-2198	19970513	<--
PRAI	US 1994-339051	A	19941114	<--		
	US 1995-539410	A	19951106	<--		
	WO 1995-US14700	W	19951113	<--		

OS MARPAT 125:114688
GI



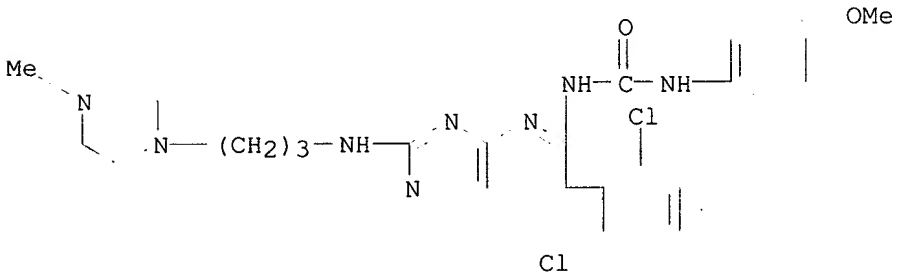
AB 6-Arylpyrido[2,3-d]pyrimidines and naphthyridines I [X = CH, N; B = halo, OH, NR3R4; R1, R2, R3, R4 = H, C1-8 alkyl, C2-8 alkenyl, C2-8 alkynyl, Ar', amino, C1-8 alkylamino, di-C1-8 alkylamino, wherein the alkyl,

alkenyl, and alkynyl groups may be substituted by amino, OH, or 5- or 6-membered carbocyclic or heterocyclic ring; Ar, Ar' = (un)substituted arom. or heteroarom. groups; R1R2N or R3R4N can complete a ring having 3-6 C atoms and optionally contg. 1 or 2 heteroatoms; when X = N and B = NR3R4, one of R3 and R4 .noteq. H] or their pharmaceutically acceptable acid and base addn. salts, useful as inhibitors of protein tyrosine **kinase** and thus useful in treating cellular **proliferation** mediated thereby, are claimed. The compds. are esp. useful in treating atherosclerosis, restenosis, psoriasis, as well as bacterial infections. In an example, the IC50 of I [X = N, B = NHCONH2, R1 = H, R2 = Et2N(CH2)4 Ar = 2,6-Cl2C6H3; prepn. given] for inhibition of protein tyrosine **kinases** was 0.231 .mu.M for PDGF and 0.0954 for FGF.

IT **179342-64-4P 179342-65-5P 179342-66-6P**
179342-67-7P 179342-68-8P 179342-69-9P
179342-71-3P 179342-73-5P 179342-74-6P
179342-76-8P
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of aryl pyridopyrimidines and naphthyridines for inhibiting protein tyrosine **kinase**-mediated cellular **proliferation**)

IT **179342-64-4P**
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of aryl pyridopyrimidines and naphthyridines for inhibiting protein tyrosine **kinase**-mediated cellular **proliferation**)

RN 179342-64-4 HCAPLUS
CN Urea, N-[6-(2,6-dichlorophenyl)-2-[[3-(4-methyl-1-piperazinyl)propyl]amino]pyrido[2,3-d]pyrimidin-7-yl]-N'-(4-methoxyphenyl)- (9CI) (CA INDEX NAME)



L67 ANSWER 15 OF 19 HCAPLUS COPYRIGHT 2002 ACS
AN 1995:777654 HCAPLUS
DN 123:198839
TI Preparation of indolocarbazole derivatives to treat prostatic **cancer** and hypertrophy
IN Dionne, Craig A.; Contreras, Patricia C.; Murakata, Chikara
PA Cephalon, Inc., USA; Kyowa Hakko Kogyo Co., Ltd.
SO PCT Int. Appl., 95 pp.
CODEN: PIXXD2
DT **Patent**
LA English
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9427982	A1	19941208	WO 1994-US6082	19940527 <--

```
        W:  AU, CA, FI, HU, JP, KR, LK, NO, NZ, PL, RO, RU, UA
        RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE
     CA 2163904        AA   19941208       CA 1994-2163904   19940527 <--
     AU 9469607        A1   19941220       AU 1994-69607     19940527 <--
     AU 679752         B2   19970710
     EP 699204         A1   19960306       EP 1994-918168    19940527 <--
     EP 699204         B1   19980415
        R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE
     EP 839814         A2   19980506       EP 1998-200023    19940527 <--
     EP 839814         A3   19980916
        R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE
     AT 165097         E    19980515       AT 1994-918168    19940527 <--
     ES 2118414        T3   19980916       ES 1994-918168    19940527 <--
     JP 2002504064     T2   20020205       JP 1995-501026    19940527 <--
     FI 9505709        A    19960103       FI 1995-5709      19951127 <--
     NO 9504816        A    19960126       NO 1995-4816      19951127 <--
PRAI US 1993-69178     A    19930528  <--
     US 1993-96622     A    19930722  <--
     EP 1994-918168    A3   19940527  <--
     WO 1994-US6082    W    19940527  <--
OS   MARPAT 123:198839
GI
```

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The title compds. [I; R = OH, alkoxy, acyloxy; R1, R2, R5, R6 = H, Cl, F, Br, I, NO2, CN, substituted ureido, etc.; X = H, CONHPh, etc.; Z1, Z2 = H, O (when combined)] [II; R1, R2, R5, R6 = H, halogen, NO2, CN, OH, substituted ureido; R3, R4 = H. alkyl, hydroxyalkyl, alkenyl; Z1, Z2 = H, O (when combined)], useful as inhibitors of tyrosine **kinase** activity assocd. with neurotropin receptors for treating benign prostatic hypertrophy or prostate **cancer**, are prepd. Thus, oxadiazepine I (R = OH, R1 = R2 = R5 = R6 = Z1 = Z2 = H, X = CONHCH2CH2OH) was prepd. and demonstrated a IC50 of 0.038 .mu.M against the Tsu-Pr1 human prostate **cancer** cell line.

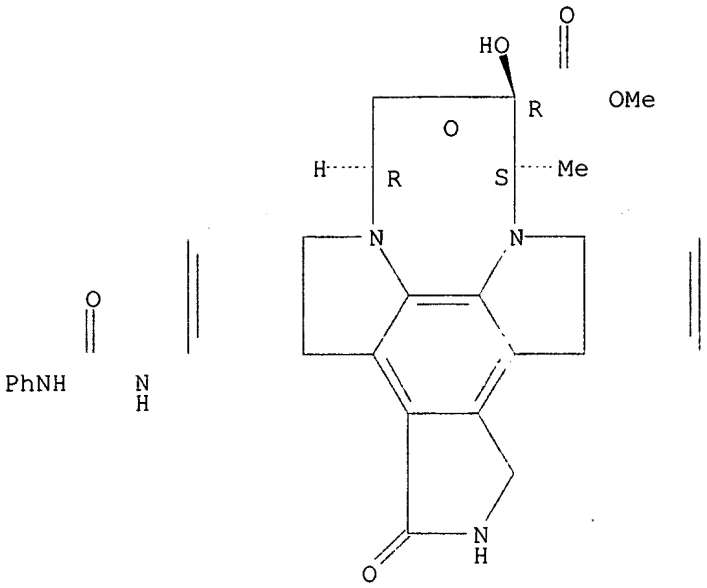
IT **121664-76-4**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(claimed compd.; prepn. of indolocarbazole derivs. to treat prostatic **cancer** and benign prostatic hypertrophy)

IT **121664-76-4**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(claimed compd.; prepn. of indolocarbazole derivs. to treat prostatic **cancer** and benign prostatic hypertrophy)

RN 121664-76-4 HCAPLUS

CN 9,12-Epoxy-1H-diindolo[1,2,3-fg:3',2',1'-kl]pyrrolo[3,4-i][1,6]benzodiazocine-10-carboxylic acid, 2,3,9,10,11,12-hexahydro-10-hydroxy-9-methyl-1-oxo-16-[[(phenylamino)carbonyl]amino]-, methyl ester, (9S,10R,12R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L67 ANSWER 16 OF 19 HCAPLUS COPYRIGHT 2002 ACS
AN 1994:400902 HCAPLUS
DN 121:902
TI Therapeutic-binding protein conjugate for inhibitor of vascular smooth muscle cells
IN Kunz, Lawrence Leroy
PA Neorx Corp., USA
SO PCT Int. Appl., 104 pp.
CODEN: PIXXD2
DT **Patent**
LA English
FAN.CNT 12

	PATENT NO.	KIND	DATE		APPLICATION NO.	DATE	
PI	WO 9407529	A1	19940414		WO 1992-US8220	19920925	<--
	W: CA, JP, US						
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, SE						
	EP 752885	A1	19970115		EP 1994-911762	19920925	<--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, SE						
	US 6251920	B1	20010626		US 1998-82643	19980521	<--
	US 6262079	B1	20010717		US 1999-306606	19990506	<--
	US 6268390	B1	20010731		US 1999-470662	19991222	<--
	US 2002013275	A1	20020131		US 2001-910388	20010720	<--
	US 2002040064	A1	20020404		US 2001-910387	20010720	<--
PRAI	US 1991-767254	A2	19910927	<--			
	WO 1992-US8220	W	19920925	<--			
	US 1993-11669	B2	19930128	<--			
	US 1993-61714	B2	19930513	<--			
	US 1993-62451	B2	19930513	<--			
	US 1994-241844	B2	19940512	<--			
	US 1994-242161	A2	19940512	<--			
	US 1995-389712	A1	19950215	<--			
	US 1995-450793	A1	19950525	<--			
	US 1995-486334	A3	19950607	<--			
	US 1998-82643	A1	19980521				
	US 1998-113733	A1	19980710				
	US 1999-470662	A1	19991222				

AB Methods are provided for inhibiting stenosis following vascular trauma or

disease in a mammalian host, comprising administering to the host a therapeutically effective dosage of a therapeutic conjugate contg. a vascular smooth muscle binding protein that assocs. in a specific manner with a cell surface of the vascular smooth muscle cell, coupled to a therapeutic agent that inhibits a cellular activity of the muscle cell. Prepn. and testing of Roridin A-monoclonal antibody conjugates is described.

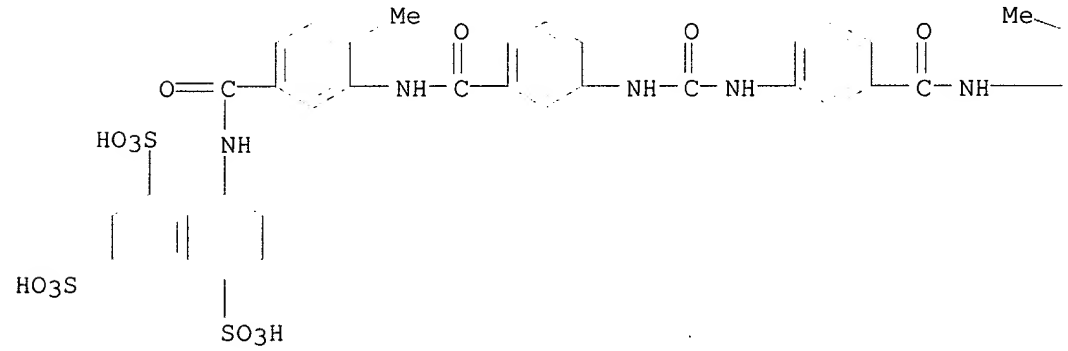
IT **145-63-1D**, Suramin, conjugates with vascular smooth muscle cell-specific binding proteins
RL: BIOL (Biological study)
(for noncytocidal vascular smooth muscle cell inhibition)

IT **145-63-1D**, Suramin, conjugates with vascular smooth muscle cell-specific binding proteins
RL: BIOL (Biological study)
(for noncytocidal vascular smooth muscle cell inhibition)

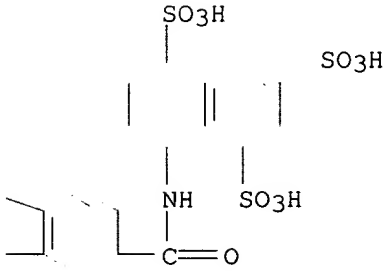
RN 145-63-1 HCAPLUS

CN 1,3,5-Naphthalenetrisulfonic acid, 8,8'-[carbonylbis[imino-3,1-phenylenecarbonylimino(4-methyl-3,1-phenylene)carbonylimino]]bis- (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 1-B

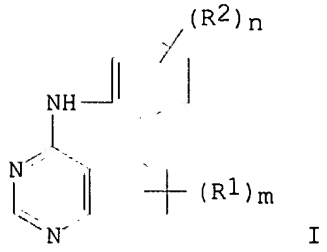


L67 ANSWER 17 OF 19 HCAPLUS COPYRIGHT 2002 ACS
AN 1994:217715 HCAPLUS

DN 120:217715
TI Quinazoline tyrosine **kinase**-inhibiting **anticancer** agents
IN Barker, Andrew J.
PA Zeneca Ltd., UK
SO Can. Pat. Appl., 99 pp.
CODEN: CPXXEB
DT **Patent**
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
PI	CA 2086968	AA	19930721	CA 1993-2086968	19930108	<--
	CA 2086968	C	19980623			
	ZA 9300015	A	19930720	ZA 1993-15	19930104	<--
	AU 9331010	A1	19930722	AU 1993-31010	19930104	<--
	AU 661533	B2	19950727			
	HU 63153	A2	19930728	HU 1993-94	19930115	<--
	EP 566226	A1	19931020	EP 1993-300270	19930115	<--
	EP 566226	B1	19951108			
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE					
	AT 130000	E	19951115	AT 1993-300270	19930115	<--
	ES 2078798	T3	19951216	ES 1993-300270	19930115	<--
	CZ 282038	B6	19970416	CZ 1993-43	19930118	<--
	NO 9300178	A	19930721	NO 1993-178	19930119	<--
	RU 2127263	C1	19990310	RU 1993-4423	19930119	<--
	SK 281551	B6	20010510	SK 1993-16	19930119	<--
	IL 104479	A1	19991222	IL 1993-104479	19930121	<--
	JP 06073025	A2	19940315	JP 1993-26577	19930216	<--
	JP 2994165	B2	19991227			
	US 5457105	A	19951010	US 1994-284293	19940802	<--
	US 5616582	A	19970401	US 1995-490666	19950615	<--
PRAI	GB 1992-1095	A	19920120	<--		
	GB 1992-13572	A	19920626	<--		
	GB 1992-23735	A	19921112	<--		
	US 1993-5280	B1	19930119	<--		
	US 1994-284293	A1	19940802	<--		

OS MARPAT 120:217715
GI



I

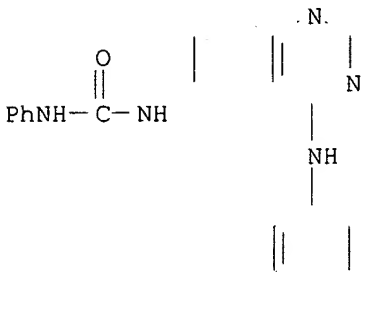
AB The title compds. I [R1 = HO, (un)substituted amino, carboxy, carbamoyl, ureido, etc.; R2 = H, HO, halogen, CF3, NH2, NO2, CN, (un)substituted C1-4 alkyl, etc.; m = 1-3; n = 1, 2], useful as tyrosine **kinase** -inhibiting **anticancer** agents (no data), are prepd. and I-contg. formulations presented. Thus, 4-chloro-6,7-dimethoxyquinazoline was condensed with 3-MeC6H4NH2, producing 6,7-dimethoxy-4-(3'-methylanilino)quinazoline hydrochloride, m.p. 248-249.degree..
IT **153437-28-6P**

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation) (prepn. of, as tyrosine **kinase**-inhibiting **anticancer** agent)

IT **153437-28-6P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation) (prepn. of, as tyrosine **kinase**-inhibiting **anticancer** agent)

RN 153437-28-6 HCAPLUS

CN Urea, N-[4-[(3-methylphenyl)amino]-6-quinazolinyl]-N'-phenyl- (9CI) (CA INDEX NAME)



L67 ANSWER 18 OF 19 HCAPLUS COPYRIGHT 2002 ACS

AN 1993:167454 HCAPLUS

DN 118:167454

TI Antibodies against the **urokinase** plasminogen activator receptor (u-PAR) and their use

IN Danoe, Keld; Roenne, Ebbe; Behrendt, Niels; Ellis, Vincent; Hoeyer-Hansen, Gunilla; Pyke, Charles; Bruenner, Nils

PA Cancerforskningsfondet af 1989, Den.

SO PCT Int. Appl., 215 pp.
CODEN: PIXXD2

DT **Patent**

LA English

FAN.CNT 4

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
PI	WO 9207083	A1	19920430	WO 1991-DK319	19911018	<--
	W: AU, CA, FI, HU, JP, KR, NO, SU, US					
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, NL, SE					
	AU 9187572	A1	19920520	AU 1991-87572	19911018	<--
	AU 661978	B2	19950817			
	EP 574391	A1	19931222	EP 1991-918632	19911018	<--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE					
	JP 07500486	T2	19950119	JP 1991-517643	19911018	<--
	WO 9308301	A1	19930429	WO 1992-DK306	19921019	<--
	W: AU, BB, BG, BR, CA, CS, FI, HU, JP, KP, KR, LK, MG, MN, MW, NO, PL, RO, RU, SD, US					
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, SN, TD, TG					
	AU 9229412	A1	19930521	AU 1992-29412	19921019	<--
	EP 637967	A1	19950215	EP 1992-923698	19921019	<--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, SE					
	US 6113897	A	20000905	US 1995-580166	19951228	<--
PRAI	WO 1990-DK270	A	19901018	<--		
	DK 1992-564		19920430	<--		
	US 1989-334613	A2	19890407	<--		
	US 1989-374854	B2	19890703	<--		
	WO 1990-DK90	A1	19900409	<--		

WO 1991-DK319 A 19911018 <--
US 1991-824189 B2 19911206 <--
WO 1992-DK306 A 19921019 <--
US 1993-85122 A3 19930617 <--

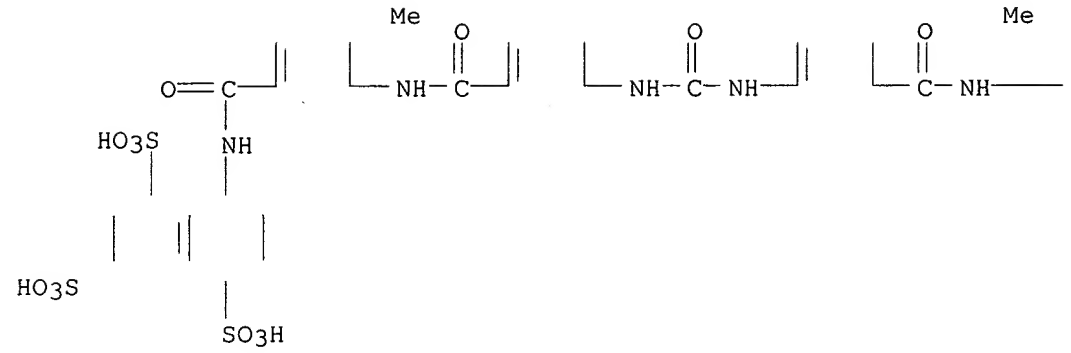
AB Monoclonal and polyclonal antibodies are provided which are directed against u-PAR or a subsequence, analog, or glycosylation variant thereof. Antibodies are disclosed which react with free u-PAR or with complexes between u-PA and u-PAR which can (1) catch u-PAR in an ELISA; (2) detect u-PAR, e.g. in blotting; (3) in radioimmunopptn. assay ppt. purified u-PAR in intact or fragment form; (4) detect u-PAR immunohistochem., e.g. in immunostaining of **cancer** cells, such as in tissue sections or at the invasive front; and (5) inhibit the binding of pro-u-PA and active u-PA and thereby inhibit cell-surface plasminogen activation. Methods are disclosed (1) for detecting or quantifying u-PAR; (2) for targeting a diagnostic to a cell contg. a u-PAR on the surface; and (3) for preventing or counteracting proteolytic activity in a mammal. Methods for selecting a substance suitable for inhibiting the u-PA/u-PAR interaction, for preventing or counteracting localized proteolytic activity in a mammal, or for inhibiting invasion and/or **metastasis** comprise the use of the antibodies and of nude mice inoculated with human **cancer** cells which are known to invade and/or **metastasize** in mice and having a distinct color (produced by an enzyme and chromogenic substrate) which is different from that of the cells of the mouse. Prepn. of the antibodies is described, as are isolation and characterization of u-PAR from U937 cells and immunochem. procedures using the antibodies. Monoclonal antibodies against u-PA inhibited the invasive and **metastatic** process in mice.

IT **145-63-1**, Suramin
RL: PRP (Properties)
(**urokinase**-type plasminogen activator interaction with receptor in presence of, immunochem. screening assay for, antibodies for)

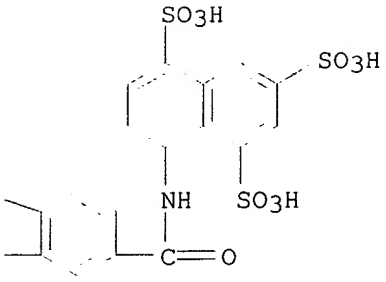
IT **145-63-1**, Suramin
RL: PRP (Properties)
(**urokinase**-type plasminogen activator interaction with receptor in presence of, immunochem. screening assay for, antibodies for)

RN 145-63-1 HCAPLUS
CN 1,3,5-Naphthalenetrisulfonic acid, 8,8'-[carbonylbis[imino-3,1-phenylenecarbonylimino(4-methyl-3,1-phenylene)carbonylimino]]bis- (9CI) (CA INDEX NAME)

PAGE 1-A



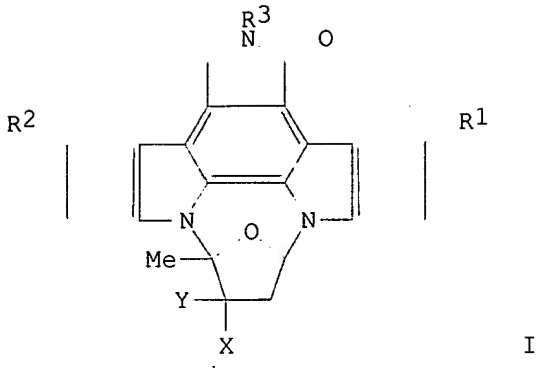
PAGE 1-B



L67 ANSWER 19 OF 19 HCAPLUS COPYRIGHT 2002 ACS
AN 1989:477750 HCAPLUS
DN 111:77750
TI K-252 derivatives as protein **kinase** C inhibitors, their preparation, and formulations containing them
IN Hirata, Tadashi; Mochida, Kenichi; Muragata, Tsutomu; Takahashi, Mitsuru; Kase, Hiroshi; Yamada, Koji; Iwahashi, Kazuyuki; Sato, Akira; Kasai, Masaji; et al.
PA Kyowa Hakko Kogyo Co., Ltd., Japan
SO Jpn. Kokai Tokkyo Koho, 40 pp.
CODEN: JKXXAF
DT **Patent**
LA Japanese
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	JP 63295588	A2	19881201	JP 1987-327858	19871224 <--
	JP 08026036	B4	19960313		
PRAI	JP 1987-12719		19870122 <--		

OS MARPAT 111:77750
GI



I

AB The title compds. I [R1,R2 = H, Me, hydroxymethyl, lower alkoxymethyl, alkylthiomethyl, etc.; R3 = H, Cl, lower alkanoyl, carbamoyl, etc.; X = hydroxymethyl, CO2H, lower alkoxycarbonyl, etc.; Y = OH, lower alkanoyloxy, etc., or YX = OCMe2OCH2, OCSNHCH2, etc.; provisos are given (for example, when X = hydroxymethyl, CO2H, lower alkoxycarbonyl, at least one of R1-R3 must be other than H)], useful as protein **kinase** C inhibitors, were prepd. Treatment of I (R1 = NH2, R2 = H, R3 = Ac, X = CO2Me, Y = OAc) (prepn. given) with MeONa, followed by workup and acidification, gave I.HCl (R1 = NH2, R2 = R3 = H, X = CO2Me, Y = OH) (II). II in vitro exhibited an IC50 of 0.175 .mu.g/mL against protein **kinase** C. A tablet formulation contg. I (R1 = R2 = R3 = H, X = CH:NOH, Y = OH) 100, starch 18, lactose 40, Ca CM-cellulose 10 g, hydroxypropylcellulose, and Mg stearate (amt. unspecified) is given.

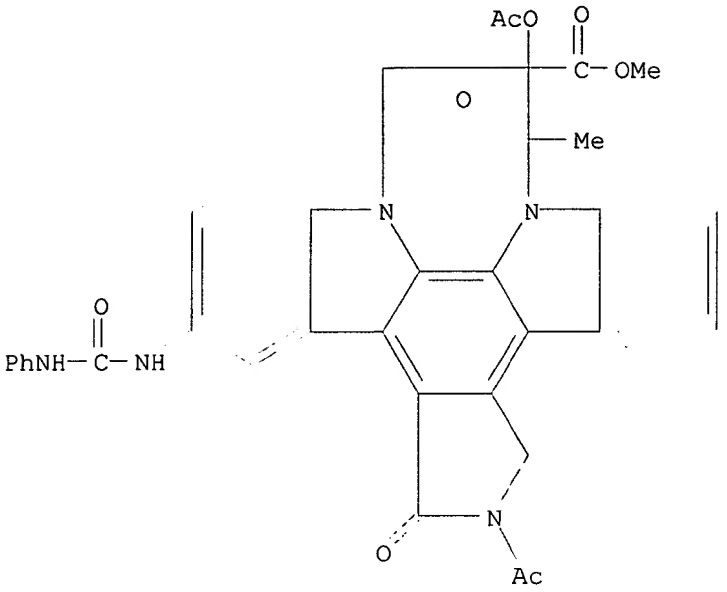
IT **121665-13-2P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and reaction of, in prepn. of protein **kinase** C inhibitor)

IT **121664-76-4P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as protein **kinase** C inhibitor)

IT **121665-13-2P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and reaction of, in prepn. of protein **kinase** C inhibitor)

RN 121665-13-2 HCAPLUS

CN 9,12-Epoxy-1H-diindolo[1,2,3-fg:3',2',1'-kl]pyrrolo[3,4-i][1,6]benzodiazocine-10-carboxylic acid, 2-acetyl-10-(acetyloxy)-2,3,9,10,11,12-hexahydro-9-methyl-1-oxo-16-[[(phenylamino)carbonyl]amino]-, methyl ester (9CI) (CA INDEX NAME)



=> d l74 bib abs hitrn fhitstr tot

L74 ANSWER 1 OF 15 HCAPLUS COPYRIGHT 2002 ACS
AN 2002:241346 HCAPLUS
DN 136:279203
TI Substituted phenyl derivatives, their preparation and use
IN Dahl, Bjarne H.; Christophersen, Palle
PA Den.
SO U.S. Pat. Appl. Publ., 21 pp., Cont.-in-part of U.S. Ser. No. 837,166.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 4

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
PI	US 2002037905	A1	20020328	US 2001-923458	20010808	<--
	WO 9847879	A1	19981029	WO 1998-DK162	19980421	<--
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM					
	RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG					
	AU 9869196	A1	19981113	AU 1998-69196	19980421	<--
	AU 728520	B2	20010111			
	EP 977741	A1	20000209	EP 1998-914851	19980421	<--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO					
	BR 9808938	A	20000801	BR 1998-8938	19980421	<--
	JP 2001521532	T2	20011106	JP 1998-544759	19980421	<--
	US 6297261	B1	20011002	US 1999-402165	19990930	<--
	WO 2000024707	A1	20000504	WO 1999-DK575	19991019	
	W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA,					

MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI,
SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM,
AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE,
DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF,
CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

	US 2002032210	A1	20020314	US 2001-837166	20010419
PRAI	DK 1997-452	A	19970422	<--	
	WO 1998-DK162	W	19980421		
	DK 1998-1362	A	19981022		
	US 1999-402165	A2	19990930		
	WO 1999-DK575	A1	19991019		
	US 2001-837166	A2	20010419		

GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Title compds. [I; 1 of R1-R3 = acidic functional group having pKa < 8 or a group convertible in vivo to such a group; R4, R5 and the others of R1-R3 = independently H, alkyl, alkoxy, OH, halo, CF3, cyano, NO2, amino, etc.; Y = C(X)NR0, NR0C(X)NR00, etc.; R0, R00 = independently H, alkyl; X = O, S; R11-R15 = independently H, alkyl, alkoxy, OH, halo, CF3, cyano (substituted) aryl, heteroaryl, phenylamino, etc.] were prepd. Thus, 3-Trifluoromethylphenyl isocyanate and 2-aminobenzoic acid were stirred in PhMe to give N-3-trifluoromethylphenyl, N'-2-carboxyphenyl urea (II). The compds. are useful as chloride channel blockers. N-3-trifluoromethylphenyl-N'-[4'-(dimethylsulfamoyl)-2-(1H-tetrazol-5-yl)-4-biphenyl]urea (III) blocked erythrocyte chloride channels with KD = 0.3 .mu.M.

IT **265646-59-1P 405520-02-7P**
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(prepn. of diarylureas and related compds. as chloride channel blockers)

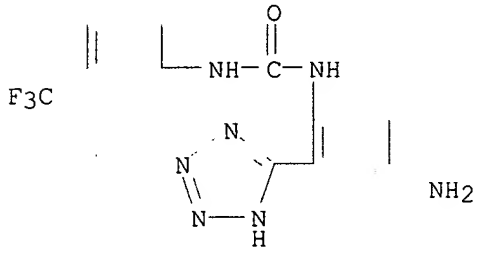
IT **1566-81-0P 2164-95-6P 200193-42-6P**
265646-51-3P 265646-52-4P 265646-53-5P
265646-54-6P 265646-55-7P 265646-57-9P
265646-60-4P 265646-61-5P 265646-62-6P
265646-63-7P 265646-64-8P 265646-65-9P
265646-66-0P 265646-67-1P 265646-68-2P
265646-69-3P 265646-71-7P 265646-72-8P
265646-75-1P 265646-76-2P 265646-77-3P
265646-78-4P 265646-79-5P 265646-80-8P
265646-81-9P 265646-82-0P 265646-83-1P
265646-84-2P 265646-85-3P 265646-86-4P
265646-87-5P 265646-88-6P 265646-89-7P
265646-90-0P 265646-91-1P 265646-92-2P
265646-94-4P 265646-95-5P 265646-96-6P
265646-97-7P 265646-98-8P 265646-99-9P
265647-00-5P 265647-01-6P 265647-02-7P
265647-03-8P 265647-04-9P 265647-06-1P
265647-07-2P 343630-41-1P 405519-92-8P
405519-93-9P 405519-94-0P 405519-96-2P
405519-98-4P 405519-99-5P 405520-00-5P
405520-01-6P 405520-03-8P 405520-04-9P
405520-05-0P 405520-06-1P 405520-07-2P
405520-08-3P 405520-09-4P 405520-10-7P
405520-11-8P 405520-12-9P 405520-13-0P
405520-69-6P 405520-74-3P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of diarylureas and related compds. as chloride channel blockers)

IT **405520-70-9**
RL: RCT (Reactant); RACT (Reactant or reagent)
(prepn. of diarylureas and related compds. as chloride channel blockers)

IT **265646-59-1P**
RL: PAC (Pharmacological activity); RCT (Reactant); **THU (Therapeutic use)**; **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(prepn. of diarylureas and related compds. as chloride channel blockers)

RN 265646-59-1 HCAPLUS
CN Urea, N-[4-amino-2-(1H-tetrazol-5-yl)phenyl]-N'-[3-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)



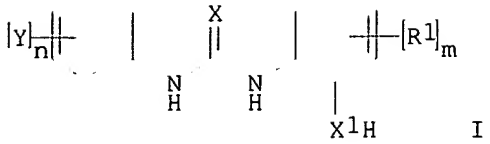
L74 ANSWER 2 OF 15 HCAPLUS COPYRIGHT 2002 ACS
AN 2001:521916 HCAPLUS
DN 135:107152
TI Preparation of N,N'-diphenyl ureas as IL-8 receptor antagonists
IN Widdowson, Katherine Louisa; Veber, Daniel Frank; Jurewicz, Anthony Joseph; Hertzberg, Robert Philip; Rutledge, Melvin Clarence, Jr.
PA Smithkline Beecham Corp., USA
SO U.S., 51 pp., Cont.-in-part of U.S. 58,86,044.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 4

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 6262113	B1	20010717	US 1998-125279	19980814 <--
US 5886044	A	19990323	US 1996-641990	19960320 <--
WO 9729743	A1	19970821	WO 1996-US13632	19960821 <--

W: AL, AM, AU, BB, BG, BR, CA, CN, CZ, EE, GE, HU, IL, IS, JP, KG, KP, KR, LK, LR, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, TR, TT, UA, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG

PRAI US 1996-641990	A2	19960320	<--
WO 1996-US13632	W	19960821	<--
US 1995-390260	B2	19950217	<--
WO 1996-US2260	A	19960216	<--

OS MARPAT 135:107152
GI



I

AB The title compds. [I; X = O; X1 = O, S; R1 = H, halo, NO2, etc.; two R1 moieties together may form O(CH2)sO, 5-6 membered unsatd. ring; s = 1-3; Y = H, halo, NO2, etc.; two Y moieties together may form O(CH2)sO, 5-6 membered unsatd. ring; n, m = 1-3], useful for treating a chemokine mediated disease, wherein the chemokine is one which binds to an IL-8 .alpha. or .beta. receptor, were prepd. Thus, reacting Me 4-amino-3-hydroxybenzoate with Ph isocyanate afforded 90% I [X = O; R = OH; R1 = 4-CO2Me; m = 1; Y = H]. All of the exemplified compds. I showed an IC50 from about 45 to about < 1 .mu.g/mL against IL-8 receptor binding. All of these compds. were also found to be inhibitors of Gro-.alpha. binding at about the same level.

IT **160383-79-9P 182497-99-0P 182498-47-1P**
182498-79-9P 182498-99-3P 182499-02-1P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(prepn. of N,N'-diphenyl ureas as IL-8 receptor antagonists)

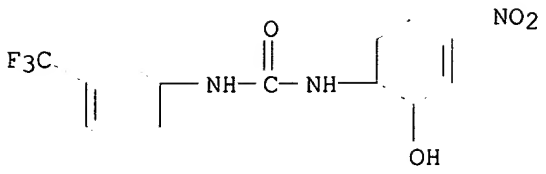
IT **85915-46-4P 88846-90-6P 92949-89-8P**
117745-32-1P 160383-78-8P 160383-90-4P
182498-03-9P 182498-07-3P 182498-11-9P
182498-15-3P 182498-18-6P 182498-20-0P
182498-22-2P 182498-25-5P 182498-26-6P
182498-28-8P 182498-30-2P 182498-31-3P
182498-32-4P 182498-33-5P 182498-34-6P
182498-35-7P 182498-38-0P 182498-40-4P
182498-42-6P 182498-44-8P 182498-45-9P
182498-46-0P 182498-48-2P 182498-50-6P
182498-52-8P 182498-54-0P 182498-55-1P
182498-57-3P 182498-59-5P 182498-62-0P
182498-63-1P 182498-64-2P 182498-66-4P
182498-67-5P 182498-68-6P 182498-69-7P
182498-70-0P 182498-71-1P 182498-72-2P
182498-73-3P 182498-74-4P 182498-75-5P
182498-76-6P 182498-77-7P 182498-78-8P
182498-81-3P 182498-82-4P 182498-83-5P
182498-84-6P 182498-85-7P 182498-86-8P
182498-87-9P 182498-88-0P 182498-89-1P
182498-90-4P 182498-91-5P 182498-92-6P
182498-93-7P 182498-94-8P 182498-95-9P
182498-97-1P 182498-98-2P 182499-00-9P
182499-01-0P 182499-03-2P 182499-05-4P
182499-06-5P 182499-07-6P 182499-08-7P
182499-09-8P 182499-10-1P 182499-11-2P
182499-12-3P 182499-13-4P 182499-14-5P
182499-15-6P 182499-16-7P 182499-17-8P
182499-18-9P 182499-19-0P 182499-20-3P
182499-21-4P 182499-22-5P 182499-23-6P
182499-25-8P 182499-26-9P 182499-27-0P
182499-28-1P 182499-29-2P 182499-30-5P
182499-31-6P 182499-32-7P 182499-33-8P
182499-34-9P 182499-35-0P 182499-36-1P
182499-37-2P 182499-38-3P 182499-39-4P
182499-40-7P 182499-41-8P 182499-42-9P

182499-43-0P 182499-44-1P 182499-45-2P
182499-46-3P 182499-47-4P 182499-48-5P
182499-49-6P 182499-50-9P 182499-51-0P
182499-52-1P 182499-53-2P 182499-54-3P
182499-55-4P 182499-56-5P 182499-57-6P
182499-58-7P 182499-59-8P 182499-60-1P
182499-61-2P 182499-62-3P 182499-63-4P
182499-64-5P 182499-65-6P 182499-66-7P
182499-67-8P 182499-68-9P 182499-69-0P
182499-70-3P 182499-71-4P 182499-72-5P
182501-57-1P 182700-31-8P 210358-24-0P
210358-26-2P 210358-29-5P 210358-30-8P
210358-31-9P 210358-32-0P 210358-33-1P
210358-34-2P 210358-35-3P 210358-36-4P
210358-37-5P 210358-38-6P 210358-39-7P
210358-40-0P 210358-41-1P 210358-42-2P
210358-43-3P 210358-44-4P 210358-45-5P
210358-46-6P 210358-47-7P 210358-48-8P
210358-49-9P 210358-50-2P 210358-51-3P
210358-52-4P 210358-53-5P 210358-54-6P
210358-55-7P 210358-56-8P 210358-57-9P
210358-59-1P 210358-60-4P 210358-61-5P
210358-62-6P 210358-63-7P 210358-64-8P
210358-66-0P 210358-67-1P 210358-68-2P
210358-69-3P 210358-70-6P 210358-71-7P
210358-72-8P 210358-73-9P 210358-74-0P
210358-75-1P 210358-77-3P 210358-78-4P
210358-79-5P 210358-80-8P 210358-81-9P
210358-84-2P 210358-86-4P 210358-88-6P
210358-93-3P 210358-95-5P 210358-97-7P
210358-98-8P 210358-99-9P 210359-00-5P
210359-01-6P 210359-02-7P 210359-03-8P
210359-04-9P 210359-05-0P 210359-06-1P
210359-07-2P 210359-08-3P 222172-42-1P
313688-79-8P 313688-80-1P 350044-75-6P
350044-78-9P 350044-79-0P 350044-80-3P
350044-81-4P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of N,N'-diphenyl ureas as IL-8 receptor antagonists)

IT **182499-76-9P 182499-79-2P 182499-88-3P**
182500-24-9P 182500-25-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of N,N'-diphenyl ureas as IL-8 receptor antagonists)

IT **160383-79-9P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); **THU (Therapeutic use)**; **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(prepn. of N,N'-diphenyl ureas as IL-8 receptor antagonists)

RN 160383-79-9 HCAPLUS
CN Urea, N-(2-hydroxy-4-nitrophenyl)-N'-[3-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)

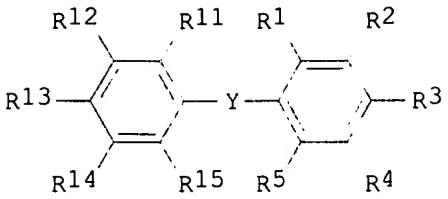


RE.CNT 57 THERE ARE 57 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L74 ANSWER 3 OF 15 HCAPLUS COPYRIGHT 2002 ACS
AN 2000:290984 HCAPLUS
DN 132:308142
TI Preparation of diarylureas and related compounds as chloride channel blockers.
IN Dahl, Bjarne H.; Christophersen, Palle
PA Neurosearch A/s, Den.
SO PCT Int. Appl., 45 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 4

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
PI	WO 2000024707	A1	20000504	WO 1999-DK575	19991019	
	W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM					
	RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG					
	AU 9963259	A1	20000515	AU 1999-63259	19991019	
	BR 9914638	A	20010703	BR 1999-14638	19991019	
	EP 1123274	A1	20010816	EP 1999-950505	19991019	
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI					
	US 2002032210	A1	20020314	US 2001-837166	20010419	
	NO 2001001956	A	20010420	NO 2001-1956	20010420	
	US 2002037905	A1	20020328	US 2001-923458	20010808	<--
PRAI	DK 1998-1362	A	19981022			
	DK 1997-452	A	19970422	<--		
	WO 1998-DK162	W	19980421			
	US 1999-402165	A2	19990930			
	WO 1999-DK575	W	19991019			
	US 2001-837166	A2	20010419			

OS MARPAT 132:308142
GI



I

AB Title compds. [I; 1 of R1-R3 = acidic functional group having pKa<8 or a group convertible in vivo to such a group; R4, R5 and the others of R1-R3 = H, alkyl, alkoxy, OH, halo, CF3, cyano, NO2, amino, etc.; Y = C(:X)NR0, NR0C(:X)NR00, etc.; R0, R00 = H, alkyl; X = O, S; R11-R15 = H, alkyl, alkoxy, OH, halo, CF3, cyano, (substituted) aryl, heteroaryl, phenylamino, etc.], were prepd. Thus, 3-trifluoromethylphenyl isocyanate and 2-aminobenzoic acid were stirred in PhMe to give N-3-trifluoromethylphenyl-N'-2-carboxyphenyl urea. N-3-trifluoromethylphenyl-N'-[4'-(dimethylsulfamoyl)-2-(1H-tetrazol-5-yl)-4-biphenyl]urea blocked erythrocyte chloride channels with KD = 0.3 .mu.M.

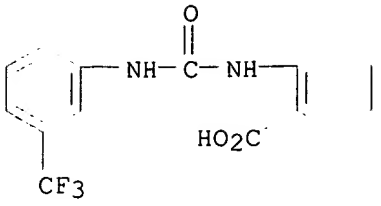
IT **1566-81-0P 2164-95-6P 200193-42-6P**
265646-51-3P 265646-52-4P 265646-53-5P
265646-54-6P 265646-55-7P 265646-57-9P
265646-59-1P 265646-60-4P 265646-61-5P
265646-62-6P 265646-63-7P 265646-64-8P
265646-65-9P 265646-66-0P 265646-67-1P
265646-68-2P 265646-69-3P 265646-70-6P
265646-71-7P 265646-72-8P 265646-73-9P
265646-74-0P 265646-75-1P 265646-76-2P
265646-77-3P 265646-78-4P 265646-79-5P
265646-80-8P 265646-81-9P 265646-82-0P
265646-83-1P 265646-84-2P 265646-85-3P
265646-86-4P 265646-87-5P 265646-88-6P
265646-89-7P 265646-90-0P 265646-91-1P
265646-92-2P 265646-94-4P 265646-95-5P
265646-96-6P 265646-97-7P 265646-98-8P
265646-99-9P 265647-00-5P 265647-01-6P
265647-02-7P 265647-03-8P 265647-04-9P
265647-07-2P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of diarylureas and related compds. as chloride channel blockers)

IT **265647-06-1P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of diarylureas and related compds. as chloride channel blockers)

IT **1566-81-0P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of diarylureas and related compds. as chloride channel blockers)

RN 1566-81-0 HCAPLUS

CN Benzoic acid, 2-[[[[3-(trifluoromethyl)phenyl]amino]carbonyl]amino]- (9CI) (CA INDEX NAME)

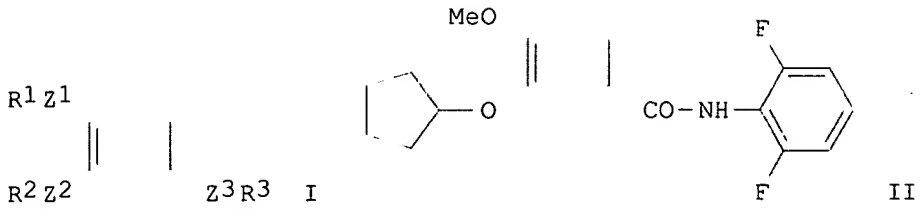


RE.CNT 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L74 ANSWER 4 OF 15 HCAPLUS COPYRIGHT 2002 ACS
AN 1999:505666 HCAPLUS
DN 131:144417
TI N-(Hetero)aryl-3,4-(cyclo)alkoxybenzamides and analogs useful as **tumor** necrosis factor and c-AMP phosphodiesterase inhibitors
IN Fenton, Garry; Morley, Andrew David; Palfreyman, Malcolm Norman; Ratcliffe, Andrew James; Harp, Brian William; Thurairatnam, Sukanthini; Vacher, Bernard Yvon Jack; Ashton, Michael John; Cook, David Charles; Hills, Susan Jacqueline; McFarlane, Ian Michael; Vicker, Nigel
PA Rhone-Poulenc Rorer Ltd., UK
SO U.S., 48 pp.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 3

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
PI	US 5935978	A	19990810	US 1993-98178	19930728	<--
	ZA 9200547	A	19930503	ZA 1992-547	19920127	<--
	WO 9212961	A1	19920806	WO 1992-GB153	19920128	<--
	W: AU, CA, CS, FI, HU, JP, KR, NO, PL, RU, US					
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, MC, NL, SE					
	AU 9211881	A1	19920827	AU 1992-11881	19920128	<--
	AU 664694	B2	19951130			
	EP 569414	A1	19931118	EP 1992-903462	19920128	<--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE					
	JP 06504782	T2	19940602	JP 1992-503280	19920128	<--
	PL 169994	B1	19960930	PL 1992-300142	19920128	<--
	CZ 281894	B6	19970312	CZ 1993-1528	19920128	<--
	NO 9302701	A	19930921	NO 1993-2701	19930727	<--
	ZA 9305448	A	19940519	ZA 1993-5448	19930728	<--
	FI 9500375	A	19950127	FI 1995-375	19950127	<--
	US 5679696	A	19971021	US 1995-484805	19950607	<--
	US 5698711	A	19971216	US 1995-487377	19950607	<--
	US 5840724	A	19981124	US 1997-881888	19970624	<--
	US 6255326	B1	20010703	US 1999-239075	19990127	<--
	US 6096768	A	20000801	US 1999-301877	19990429	<--
PRAI	GB 1991-1777	A	19910128	<--		
	GB 1991-17727	A	19910816	<--		
	WO 1992-GB153	B2	19920128	<--		
	GB 1992-15989	A	19920728	<--		
	GB 1992-16005	A	19920728	<--		
	GB 1992-16006	A	19920728	<--		
	GB 1992-16008	A	19920728	<--		
	GB 1992-16764	A	19920807	<--		
	GB 1993-10633	A	19930521	<--		
	GB 1993-10938	A	19930527	<--		
	GB 1993-11281	A	19930601	<--		
	GB 1993-14847	A	19930716	<--		
	US 1993-98178	A3	19930728	<--		

US 1995-484805 A3 19950607 <--
OS MARPAT 131:144417
GI



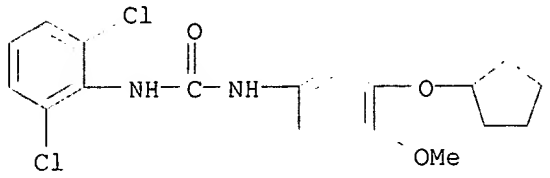
AB Title compds. (I) [R1 = lower alkyl; R2 = (un)substituted cycloalkyl, (un)substituted cycloalkenyl, (un)substituted or oxidized cyclothioalkyl, or (un)substituted or oxidized cyclothioalkenyl; R3 = (un)substituted (hetero)aryl; Z, Z1, Z2 = independently O or S; Z3 = C(:Z)NH] and their N-oxides and salts were prepd. for pharmaceutical use as **tumor** necrosis factor and cAMP phosphodiesterase inhibitors. Thus, 3-cyclopentyloxy-4-methoxybenzoyl chloride (prepn. given) in CH2Cl2 was added dropwise to 2,6-difluoroaniline in triethylamine and CH2Cl2 and refluxed for 4 h to yield N-(2,6-difluorophenyl)-3-cyclopentyloxy-4-methoxybenzamide (II). Compds. of the invention were tested for inhibitory effects on PDE activity and eosinophil superoxide generation, effects on tracheal smooth muscle contractility, in vivo bronchodilator actions and antigen(ovalbamin)-induced eosinophilia, in vitro inhibitory effects on TNF-.alpha. release by human monocytes, and inhibitory effects on antigen-induced bronchoconstriction in conscious guinea-pigs and serum TNF-.alpha. levels in LPS-challenged mice. Compds. showed 10,000-fold to 50-fold more selectivity for cAMP phosphodiesterase IV than cyclic nucleotide phosphodiesterase types I, III, or V and have IC50 values ranging from 0.1 nM to 40 .mu.M for PDE activity. At concns. from 5x10-9M to 10-5M, preferably 5x10-9 to 10-7, compds. produced about 50% relaxation of guinea-pig tracheal strips. When administered at EDs of 4 to 1000 .mu.g/kg, preferably 4 to 50 .mu.g/kg, compds. produced 30% to 90% decrease in bronchospasm without any significant effect on blood pressure. At oral doses of 1 to 50 mg/kg, preferably 1 to 10 mg/kg, and inhaled doses of 4 to 1000 .mu.g/kg, preferably 4 to 50 .mu.g/kg, compds. inhibited by at least 50% ovalbumin-induced eosinophilia in guinea-pigs. Compds. produced 50% inhibition of LPS-induced TNF-.alpha. release from human PBMs at concns. of 10-9M to 10-6M, preferably 10-9M to 10-8 M. At doses of 1 to 1000 .mu.g/kg (i.t.), preferably 1 to 20 .mu.g/kg (i.t.), compds. inhibited antigen-induced bronchoconstriction by up to 80%. Compds. inhibited LPS-induced serum TNF-.alpha. at doses of 10 to 10,000 .mu.g/kg, preferably 10 to 250 .mu.g/kg. Compds. showed very low mammalian toxicity levels. Twenty-one compns. of the title compds. for gelatin capsules or dry powder inhalers were also prepd.

IT **159782-48-6P**, N-(2,6-Dichlorophenyl)-N'-(3-cyclopentyloxy-4-methoxyphenyl)urea **159782-49-7P**, N-(3,5-Dichloropyrid-4-yl)-N'-(3-cyclopentyloxy-4-methoxyphenyl)urea
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of N-(hetero)aryl 3,4-(cyclo)alkoxybenzamides and analogs useful as **tumor** necrosis factor and c-AMP phosphodiesterase inhibitors)

IT **159782-48-6P**, N-(2,6-Dichlorophenyl)-N'-(3-cyclopentyloxy-4-methoxyphenyl)urea
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of N-(hetero)aryl 3,4-(cyclo)alkoxybenzamides and analogs useful as **tumor** necrosis factor and c-AMP phosphodiesterase inhibitors)

RN 159782-48-6 HCAPLUS
CN Urea, N-[3-(cyclopentyloxy)-4-methoxyphenyl]-N'-(2,6-dichlorophenyl)-(9CI) (CA INDEX NAME)

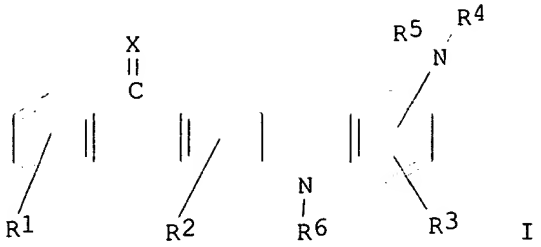


RE.CNT 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L74 ANSWER 5 OF 15 HCAPLUS COPYRIGHT 2002 ACS
AN 1998:612095 HCAPLUS
DN 129:244921
TI Preparation of aromatic sulfonyl alpha-hydroxy hydroxamic acid compounds as matrix metalloprotease inhibitors
IN Freskos, John N.; Boehm, Terri L.; Mischke, Brent V.; Heintz, Robert M.; Mcdonald, Joseph J.; Decrescenzo, Gary A.; Howard, Susan C.
PA Monsanto Company, USA
SO PCT Int. Appl., 203 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 4

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
PI	WO 9839326	A1	19980911	WO 1998-US4277	19980304	
	W: AL, AU, BA, BB, BG, BR, CA, CN, CU, CZ, EE, GE, GH, GW, HU, ID, IL, IS, JP, KP, KR, LC, LK, LR, LT, LV, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, SL, TR, TT, UA, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM					
	RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG					
	AU 9864478	A1	19980922	AU 1998-64478	19980304	<--
	AU 737329	B2	20010816			
	EP 984959	A1	20000315	EP 1998-910177	19980304	<--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI					
	BR 9808150	A	20000328	BR 1998-8150	19980304	
	US 6362183	B1	20020326	US 1999-254535	19990604	<--
PRAI	US 1997-35182P	P	19970304	<--		
	WO 1998-US4277	W	19980304			

OS MARPAT 129:244921
AB The title compds. HONHC(O)C(OH)(R2)CH2SO2R1 [I; R2 = H, C1-4 alkyl, C1-4 haloalkyl, etc.; R1 = 5-6 membered cycloalkyl, heterocyclyl, aryl, etc.] which inter alia inhibit matrix metalloprotease activity, were prepd. Thus, multi-step synthesis of I [R1 = 4-PhOC6H4; R2 = Me] which showed 51.9% inhibition of angiogenesis in the cornea of a mouse, was described.
IT **213183-96-1P 213184-00-0P 213184-01-1P**
213184-03-3P
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of arom. sulfonyl alpha-hydroxy hydroxamic acid compds. as matrix metalloprotease inhibitors)



I

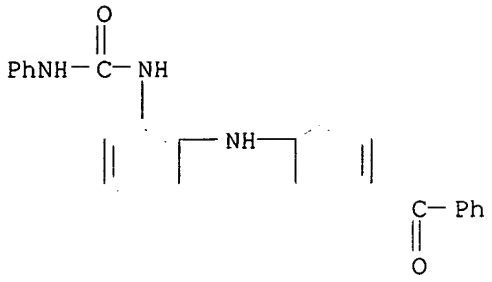
AB The title compds. I [R1 and R2 stand independently for one or more, similar or different substituents selected from the group consisting of hydrogen, halogen, hydroxy, mercapto, trifluoromethyl, amino, alkyl, alkoxy, alkylthio, alkylamino, or alkoxycarbonyl, the C-content of which can be from 1 to 5, cyano, carboxy, carbamoyl, Ph, or nitro; R3 stands for hydrogen, halogen, hydroxy, mercapto, trifluoromethyl, amino, alkyl, alkoxy, alkylthio, alkylamino, or alkoxycarbonyl, the C-content of which can be from 1 to 5, Ph, cyano, carboxy, or carbamoyl; R4, R5 and R6 stand independently for hydrogen, trifluoromethyl, alkyl, carbamoyl, alkoxycarbonyl, or alkyloxo, the C-content of which can be from 1 to 5; X stands for oxygen, NOH, NO-alkyl, dialkoxy, cyclic dialkoxy, dialkylthio, or cyclic dialkylthio, the C-content of which can be from 1 to 5] are prepd. The present compds. are of value in the human and veterinary practice as systemic and topical therapeutic agents for the treatment and prophylaxis of asthma, allergy, rheumatoid arthritis, spondyloarthritis, gout, atherosclerosis, chronic inflammatory bowel disease, **proliferative** and inflammatory skin disorders, such as psoriasis, and atopic dermatitis. In an in vitro test using human polymorphonuclear granulocytes, 4-(2-aminophenylamino)-2-chloro-2'-methylbenzophenone in vitro showed IC50 of 13 nM and 7.1 nM against the prodn. of Il-1.beta. and TNF-.alpha., resp. In the above test, 4-(2-aminophenylamino)benzophenone (II) in vitro showed IC50 of 250 nM and 790 nM against the prodn. of Il-1.beta. and TNF-.alpha., resp. In the 12-O-tetradecanoylphorbol-13-acetate induced murine skin inflammation model, II showed activity equal to hydrocortisone.

IT **210965-94-9P**
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of aminobenzophenones as inhibitors of interleukin and TNF)

IT **210965-94-9P**
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of aminobenzophenones as inhibitors of interleukin and TNF)

RN 210965-94-9 HCAPLUS

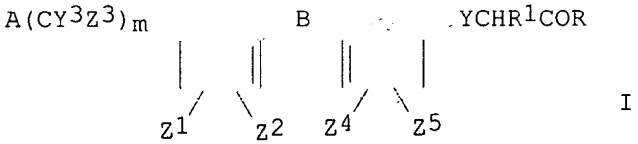
CN Urea, N-[2-[(4-benzoylphenyl)amino]phenyl]-N'-phenyl- (9CI) (CA INDEX NAME)



L74 ANSWER 7 OF 15 HCAPLUS COPYRIGHT 2002 ACS
AN 1998:430106 HCAPLUS
DN 129:108912
TI Preparation of 3-guanidinophenylamides and related compounds as integrin .alpha.v.beta.3 inhibitors or antagonists.
IN Chandrakumar, Nizal; Chen, Barbara B.; Chen, Helen Y.; Clare, Michael; Gasiecki, Alan F.; Haack, Richard A.; Malecha, James W.; Ruminski, Peter G.; Russell, Mark A.
PA G. D. Searle & Co., USA
SO U.S., 77 pp.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5773646	A	19980630	US 1997-825086	19970327 <--

OS MARPAT 129:108912
GI



AB Title compds. [I; A = NR5C(Y1)NR7R8, etc.; Y1 = NR2, O, S; R2 = H, alkyl, aryl, OH, alkoxy, cyano, NO2, amino, aminocarbonyl, alkenyl, alkynyl, (substituted) alkyl, aryl, heterocyclyl; R2R7 = (substituted) heterocyclyl; R7, R8 = H, alkyl, alkenyl, alkynyl, aralkyl, cycloalkyl, bicycloalkyl, aryl, acyl, benzoyl, (substituted) alkyl, heterocyclyl, etc.; NR7R8 = (substituted) mono- or bicyclic heterocyclyl; R5 = H, alkyl, alkenyl, alkynyl, PhCH2, PhCH2CH2; Z1, Z2, Z4, Z5 = H, alkyl, OH, alkoxy, aryloxy, aralkoxy, halo, haloalkyl, haloalkoxy, NO2, amino, aminoalkyl, alkylamino, dialkylamino, cyano, alkylthio, alkylsulfonyl, carboxyl derivs., (fused) aryl; cycloalkyl, (fused) heterocyclyl, A; B = SO2NR50, CONR50(CH2)p, CH2O, SOCH2, SO2CH2, etc.; p = 0-2; R50 = H, alkyl; Y = (CHR70)q, O; q = 0, 1; R70 = H, alkyl, (substituted) aryl; m = 0-2; R = XR3; X = O, S, NR4; R3, R4 = H, alkyl, alkenyl, alkynyl, halolalkyl, aryl, aralkyl, etc.; Y3, Z3 = H, alkyl, aryl, cycloalkyl, aralkyl; R1 = H, alkyl, aryl, etc.], were prepd. Thus, 3-[[[3-[(aminomiminomethyl)amino]phenyl]sulfonyl]amino]-.beta.-phenylbenzenepropanoic acid trifluoroacetate (prepn. given) inhibited vitronectin adhesion with IC50 = 16.7 nM.

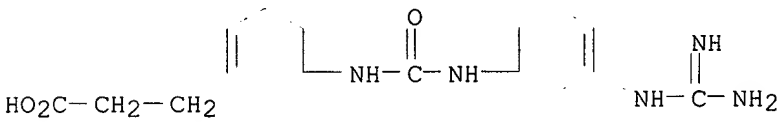
IT **197790-95-7P 197790-96-8P 197790-97-9P 197790-98-0P**

RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of 3-guanidinophenylamides and related compds. as integrin inhibitors or antagonists)

IT **197792-61-3P 197792-62-4P 197792-63-5P**
197792-64-6P 197792-65-7P 197792-66-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. of 3-guanidinophenylamides and related compds. as integrin inhibitors or antagonists)

IT **197790-95-7P**
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of 3-guanidinophenylamides and related compds. as integrin inhibitors or antagonists)

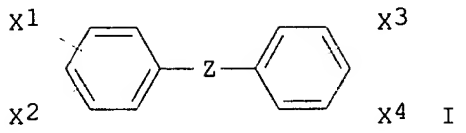
RN 197790-95-7 HCAPLUS
CN Benzenepropanoic acid, 3-[[[[3-[(aminoiminomethyl)amino]phenyl]amino]carbonyl]amino]- (9CI) (CA INDEX NAME)



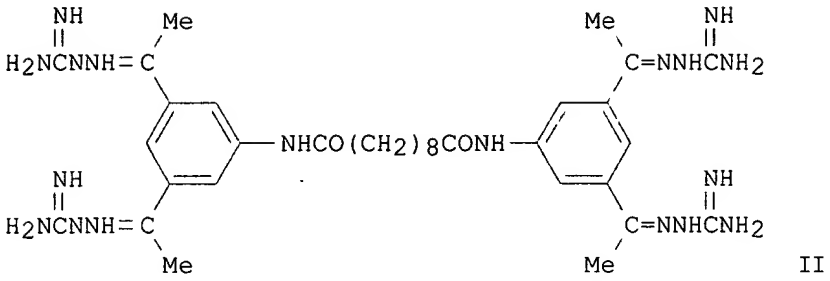
L74 ANSWER 8 OF 15 HCAPLUS COPYRIGHT 2002 ACS
AN 1998:331368 HCAPLUS
DN 129:4502
TI Preparation of guanylhydrazones and their use to treat inflammatory conditions
IN Bianchi, Marina; Cerami, Anthony; Tracey, Kevin J.; Ulrich, Peter
PA Picower Institute for Medical Research, USA
SO U.S., 44 pp. Cont.-in-part of U.S. 5,599,984.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 3

	PATENT NO.	KIND	DATE		APPLICATION NO.	DATE
PI	US 5750573	A	19980512		US 1995-463568	19950605 <--
	US 5599984	A	19970204		US 1994-315170	19940929 <--
	US 5753684	A	19980519		US 1995-471696	19950606 <--
	US 5849794	A	19981215		US 1995-472004	19950606 <--
	US 5859062	A	19990112		US 1995-471124	19950606 <--
	US 6008255	A	19991228		US 1995-471305	19950606 <--
	US 6022900	A	20000208		US 1995-471919	19950606 <--
	US 6180676	B1	20010130		US 1995-472003	19950606 <--
	US 6248787	B1	20010619		US 1995-479050	19950606 <--
	US 5854289	A	19981229		US 1996-632305	19960415 <--
	US 2002028851	A1	20020307		US 2001-824217	20010403 <--
PRAI	US 1994-184540	B2	19940121	<--		
	US 1994-315170	A2	19940929	<--		
	US 1995-463568	A3	19950605	<--		
	US 1995-479050	A1	19950606	<--		

OS MARPAT 129:4502
GI



I



II

AB Arom. guanylhydrazone (more properly termed amidinohydrazone) [I; X2 = GhyCH, GhyCCH3 or H, wherein Ghy = guanylhydrazono; X1, X3 and X4, independently = GhyCH or GhyCCH3; and Z = NH(CO)NH] are prepd. This invention concerns new methods and compns. that are useful in preventing and ameliorating cachexia, the clin. syndrome of poor nutritional status and bodily wasting assocd. with **cancer** and other chronic diseases. More particularly, the invention relates to compns. contg. amidinohydrazone I and their use to inhibit the uptake of arginine by macrophages and/or its conversion to urea. These compns. and methods are also useful in preventing the generation of nitric oxide (NO) by cells, and so to prevent NO-mediated inflammation and other responses in persons in need of same. In another embodiment, the compds. I can be used to inhibit arginine uptake in arginine-dependent **tumors** and infections. Thus, N,N'-bis(3,5-diacetylphenyl)decanediamide, aminoguanidine hydrochloride, and aminoguanidine dihydrochloride were heated in 91% ethanol for 18 h to give the title compd. (II). II was the most active compd. in vitro for inhibiting urea prodn. in RAW 264.7 cell with IC50 of 1 .mu.M.

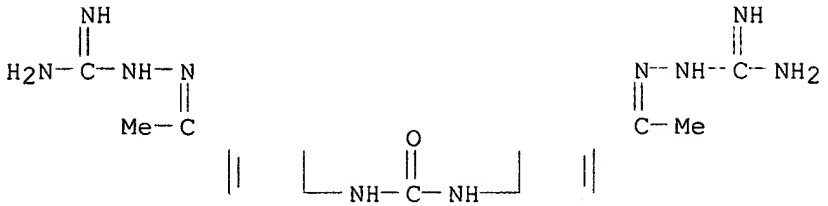
IT **15427-75-5P 169764-82-3P 169765-12-2P 169765-13-3P 187959-61-1P**
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of guanylhydrazones for treating NO- or arginine-mediated diseases such as inflammatory conditions)

IT **169765-14-4P 169765-32-6P 169765-36-0P 169765-37-1P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. of guanylhydrazones for treating NO- or arginine-mediated diseases such as inflammatory conditions)

IT **15427-75-5P**
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of guanylhydrazones for treating NO- or arginine-mediated diseases such as inflammatory conditions)

RN 15427-75-5 HCAPLUS

CN Hydrazinecarboximidamide, 2,2'-[carbonylbis(imino-4,1-phenyleneethylidyne)]bis-, dihydrochloride (9CI) (CA INDEX NAME)

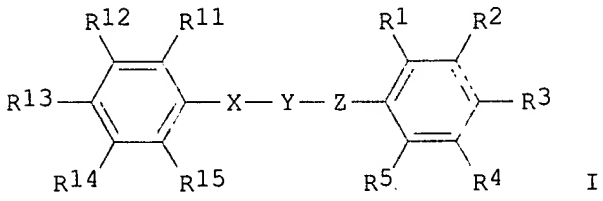


●2 HCl

L74 ANSWER 9 OF 15 HCAPLUS COPYRIGHT 2002 ACS
AN 1997:805714 HCAPLUS
DN 128:61354
TI Preparation of arylureas and related compounds as chloride channel blockers.
IN Christophersen, Palle; Pedersen, Ove
PA Neurosearch A/S, Den.; Christophersen, Palle; Pedersen, Ove
SO PCT Int. Appl., 36 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 4

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9745400	A1	19971204	WO 1997-EP2723	19970526 <--
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	AU 9729621	A1	19980105	AU 1997-29621	19970526 <--
	AU 735545	B2	20010712		
	EP 906273	A1	19990407	EP 1997-924019	19970526 <--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
	JP 2000511167	T2	20000829	JP 1997-541595	19970526 <--
PRAI	DK 1996-602	A	19960524 <--		
	DK 1997-452	A	19970422 <--		
	WO 1997-EP2723	W	19970526 <--		

OS MARPAT 128:61354
GI



I

AB Title compds. [I; 1 of R1, R2, R3 = non-cyclic acidic group having a pKa

value <8 or a group in vivo convertible thereto; R4, R5, and the other 2 of R1, R2, R3 = H, alkyl, cycloalkyl, cycloalkylalkyl, alkenyl, alkynyl, alkoxy, hydroxy, halo, CF3, OCF3, cyano, NO2, amino, (substituted) aryl, aralkyl, arylamino, aryloxy, arylcarbonyl, heteroaryl; R3R4 or R4R5 = (unsatd.) fused 4-7 membered carbocyclic ring; X = NH, CH2NH, SO2NH; Y = CO, CS, SO2, C(:NR8); R8 = H, alkyl, cyano; X = NH, CH2NH, SO2NH; Z = NR6, O, CH:CH, C.tplbond.C, N:CH, CH:N; R6 = H, alkyl; R11-R15 = H, alkyl, cycloalkyl, cycloalkylalkyl, alkenyl, alkynyl, alkoxy, OH halo, CF3, OCF3, cyano, NO2, amino, NHSO2R7, CO2R7, SO2N(R7)2, SO2OR7, etc.], were prepd. Thus, 3-trifluoromethylphenyl isocyanate and 2-aminobenzoic acid were kept in toluene to give N-(3-trifluoromethylphenyl)-N'-(2-carboxyphenyl)urea. The latter at 10 .mu.M normalized the basal K+ flux from sickle erythrocytes and nearly abolished the deoxygenation induced flux component.

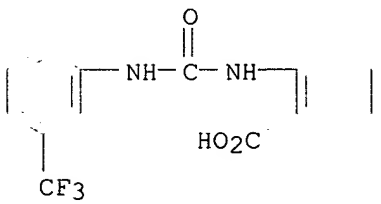
IT **1566-81-0P 1566-82-1P 1566-85-4P**
1566-86-5P 1566-88-7P 1566-98-9P
54506-39-7P 160384-12-3P 160384-14-5P
160384-23-6P 182958-17-4P 195133-45-0P
200193-39-1P 200193-40-4P 200193-41-5P
200193-42-6P 200193-43-7P 200193-44-8P
200193-45-9P 200193-46-0P 200193-47-1P
200193-48-2P 200193-49-3P 200193-50-6P
200193-52-8P 200193-53-9P 200193-56-2P
200193-57-3P 200193-58-4P 200193-59-5P
200193-60-8P 200193-62-0P 200193-63-1P
200193-64-2P 200193-65-3P
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of arylureas and related compds. as chloride channel blockers)

IT **200193-72-2**
RL: RCT (Reactant)
(prepn. of arylureas and related compds. as chloride channel blockers)

IT **200193-73-3P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. of arylureas and related compds. as chloride channel blockers)

IT **1566-81-0P**
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of arylureas and related compds. as chloride channel blockers)

RN 1566-81-0 HCAPLUS
CN Benzoic acid, 2-[[[[3-(trifluoromethyl)phenyl]amino]carbonyl]amino]- (9CI) (CA INDEX NAME)



L74 ANSWER 10 OF 15 HCAPLUS COPYRIGHT 2002 ACS
AN 1997:679052 HCAPLUS
DN 127:318772
TI Preparation of meta-substituted phenylene derivatives and their use as .alpha.v.beta.3 integrin antagonists or inhibitors
IN Chandrakumar, Nizal; Chen, Barbara B.; Chen, Helen; Clare, Michael; Gasiecki, Alan F.; Haack, Richard A.; Malecha, James W.; et al.

PA G.D. Searle & Co., USA; Chandrakumar, Nizal; Chen, Barbara B.; Chen, Helen; Clare, Michael; Gasiecki, Alan F.

SO PCT Int. Appl., 306 pp.
CODEN: PIXXD2

DT Patent

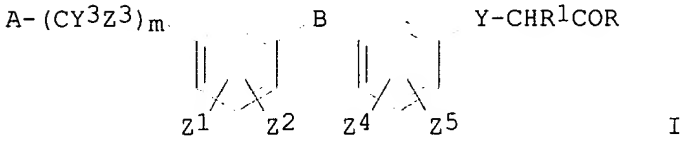
LA English

FAN.CNT 1

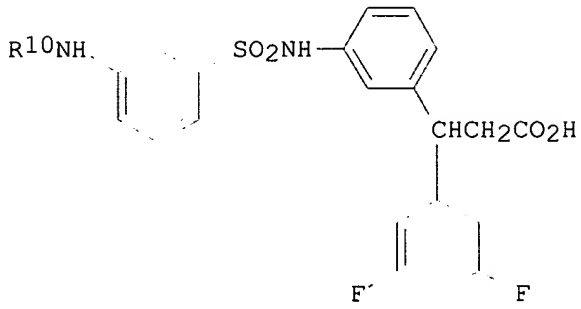
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9736862	A1	19971009	WO 1997-US4461	19970326 <--
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	CA 2250464	AA	19971009	CA 1997-2250464	19970326 <--
	AU 9723370	A1	19971022	AU 1997-23370	19970326 <--
	EP 889877	A1	19990113	EP 1997-916110	19970326 <--
	EP 889877	B1	20010829		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				
	JP 2000506538	T2	20000530	JP 1997-535309	19970326 <--
	AT 204857	E	20010915	AT 1997-916110	19970326 <--
	ES 2162676	T3	20020101	ES 1997-916110	19970326 <--
PRAI	US 1996-14464P	P	19960329 <--		
	WO 1997-US4461	W	19970326 <--		

OS MARPAT 127:318772

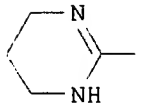
GI



I



II

Q= 

AB The present invention relates to a class of compds., i.e, phenylalkanoic acid and phenoxyacetic acid derivs., represented by formula [I; A =

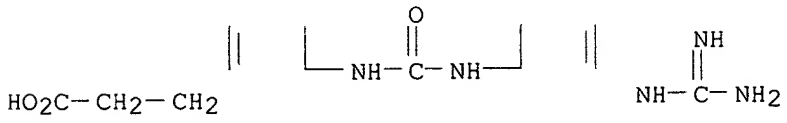
(un)substituted NHC(:NH)NH, NHCONH, NHC(:S)NH, or NHCH:NH, C(:NH)NH2, C(:NOH)NH2; Z1 - Z5 = H, alkyl, OH, alkoxy, aryloxy, aralkoxy, halo, haloalkyl, haloalkoxy, NO2, NH2, aminoalkyl, alkylamino, dialkylamino, cyano, etc.; B = N-(un)substituted CONH(CH2)p or SO2NH, NHCONH(CH2)p, CO2(CH2)p, CH2CH2, alkenylene or alkynylene optionally substituted by oxo, CH2O, SCH2, SOCH2, SO2 CH2, CH(OH)CH2O, CH:CHCO; wherein p = 0, 1,2; Y = (un)substituted (CH2)q, O; q = 0,1; m = 0, 1,2; R = X-R3; wherein X = O, S, (un)substituted NH; R3 = H, alkyl, alkenyl, alkynyl, haloalkyl, aryl, aralkyl, sugar or steroid residue; Y3, Z3 = H, alkyl, aryl, cycloalkyl, aralkyl; R1 = H, alkyl, aryl, NHCOR51, NHCO2R12, NHCOR12, NHSO2R12, NHCONHR12; wherein R12 = H, alkyl, cycloalkyl, aralkyl, aryl; R51 = N-substituted pyrrolidinyl, piperidinyl, or morpholinyl] or pharmaceutically acceptable salts thereof are prepd. Also claimed are pharmaceutical compns. comprising above compds. I and methods of selectively inhibiting or antagonizing .alpha.v.beta.3 integrin. A method for treating conditions mediated by .alpha.v.beta.3 integrin, e.g. **tumor metastasis**, solid **tumor** growth, angiogenesis, osteoporosis, humoral hypercalcemia of **malignancy**, smooth muscle cell migration, restenosis, in a mammal comprises administering an effective .alpha.v.beta.3 integrin-inhibiting amt. of above compds. I. Thus, 3-(3-aminobenzenesulfonamido)-3-phenylpropanoic acid deriv. (II; R10 = H) was condensed with N,N'-bis(tert-butoxycarbonyl)-2-(1H)-tetrahydropyrimidinethione followed by deprotection to give II (R10 = Q), which showed IC50 of 0.75 nM for 50% inhibition of the max. binding of biotinylated vitronectin to human vitronectin receptor (.alpha.v.beta.3) purified from human placenta (Niiya et al., Blood, 1987).

IT **197790-95-7P 197790-96-8P 197790-97-9P**
197790-98-0P
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of meta-substituted phenylene derivs. and their use as .alpha.v.beta.3 integrin antagonists or inhibitors for disease treatment)

IT **197792-61-3P 197792-62-4P 197792-63-5P**
197792-64-6P 197792-65-7P 197792-66-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. of meta-substituted phenylene derivs. and their use as .alpha.v.beta.3 integrin antagonists or inhibitors for disease treatment)

IT **197790-95-7P**
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of meta-substituted phenylene derivs. and their use as .alpha.v.beta.3 integrin antagonists or inhibitors for disease treatment)

RN 197790-95-7 HCAPLUS
CN Benzenepropanoic acid, 3-[[[[3-[(aminoiminomethyl)amino]phenyl]amino]carbonyl]amino]- (9CI) (CA INDEX NAME)



L74 ANSWER 11 OF 15 HCAPLUS COPYRIGHT 2002 ACS
AN 1997:679049 HCAPLUS
DN 127:346198

TI Para-substituted phenylpropanoic acid derivatives prepared as integrin antagonists

IN Chen, Barbara B.; Chen, Helen Y.; Gesicki, Glen J.; Haack, Richard A.; Malecha, James W.; Penning, Thomas D.; Rico, Joseph G.; Rogers, Thomas E.; et al.

PA G.D. Searle & Co., USA; Chen, Barbara B.; Chen, Helen Y.; Gesicki, Glen J.; Haack, Richard A.; Malecha, James W.; Penning, Thomas D.

SO PCT Int. Appl., 359 pp.
CODEN: PIXXD2

DT Patent

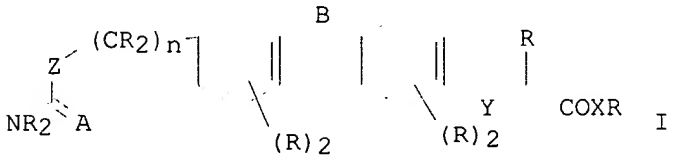
LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9736859	A1	19971009	WO 1997-US4460	19970326 <--
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	CA 2250698	AA	19971009	CA 1997-2250698	19970326 <--
	AU 9725360	A1	19971022	AU 1997-25360	19970326 <--
	EP 891325	A1	19990120	EP 1997-916852	19970326 <--
	EP 891325	B1	20020206		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				
	JP 2000515493	T2	20001121	JP 1997-535308	19970326 <--
	EP 1157985	A1	20011128	EP 2001-114256	19970326 <--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				
	US 5952381	A	19990914	US 1997-826244	19970327 <--
	US 6251944	B1	20010626	US 1999-288742	19990408 <--
PRAI	US 1996-14288P	P	19960329 <--		
	EP 1997-916852	A3	19970326 <--		
	WO 1997-US4460	W	19970326 <--		
	US 1997-826244	A3	19970327 <--		

OS MARPAT 127:346198

GI



AB The present prepn. relates to a class of racemic, L-, or D-compds. [I; A = O, S, NH, NOH, NR; R = H, OH, alkyl, aryl, nitro, amino; B = CH2CONH, COO, SO2NH, CH2O, OCH2; Z = bond, NR; Y = O, S, SO2; X = O, S, N; n = 0-2; etc.] or a pharmaceutically acceptable salt thereof, which offers treatment of disease states, including angiogenesis (no data).

IT **198150-78-6P**
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(4-substituted phenylpropanoic acid derivs. prepd. as integrin antagonists)

IT **198150-77-5P 198152-76-0P 198152-77-1P**
198152-78-2P 198152-79-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)

(4-substituted phenylpropanoic acid derivs. prepd. as integrin antagonists)

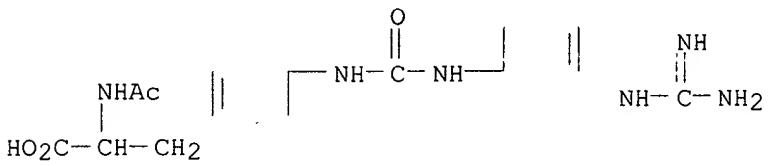
IT **198150-78-6P**
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(4-substituted phenylpropanoic acid derivs. prepd. as integrin antagonists)

RN 198150-78-6 HCAPLUS

CN Phenylalanine, N-acetyl-4-[[[[3-[(aminoiminomethyl)amino]phenyl]amino]carbonyl]amino]-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

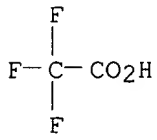
CM 1

CRN 198150-77-5
CMF C19 H22 N6 O4



CM 2

CRN 76-05-1
CMF C2 H F3 O2



L74 ANSWER 12 OF 15 HCAPLUS COPYRIGHT 2002 ACS

AN 1997:124926 HCAPLUS

DN 126:211914

TI Preparation of arylamidinohydrazones for treatment of cachexia and nitric oxide-mediated diseases.

IN Bianchi, Marina; Cerami, Anthony; Tracey, Kevin J.; Ulrich, Peter

PA Picower Institute for Medical Research, USA

SO U.S., 42 pp. Cont.-in-part of U.S. Ser. No. 184,540, abandoned.
CODEN: USXXAM

DT Patent

LA English

FAN.CNT 3

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 5599984	A	19970204	US 1994-315170	19940929 <--
CA 2181689	AA	19950727	CA 1995-2181689	19950119 <--
WO 9519767	A1	19950727	WO 1995-US828	19950119 <--

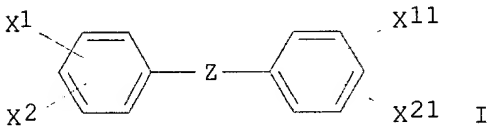
W: AM, AU, BB, BG, BR, BY, CA, CN, CZ, EE, FI, GE, HU, JP, KE, KG, KR, KZ, LK, LR, LT, LV, MD, MG, MN, MW, MX, NO, NZ, PL, RO, RU, SD, SI, SK, TJ, TT, UA, UZ, VN

RW: KE, MW, SD, SZ, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG

	AU 9518330	A1	19950808	AU 1995-18330	19950119 <--
	AU 683999	B2	19971127		
	EP 746312	A1	19961211	EP 1995-910110	19950119 <--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
	CN 1144480	A	19970305	CN 1995-192171	19950119 <--
	JP 09508123	T2	19970819	JP 1995-519690	19950119 <--
	EP 1160240	A1	20011205	EP 2001-112374	19950119 <--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE				
	US 5750573	A	19980512	US 1995-463568	19950605 <--
	US 5753684	A	19980519	US 1995-471696	19950606 <--
	US 5849794	A	19981215	US 1995-472004	19950606 <--
	US 5859062	A	19990112	US 1995-471124	19950606 <--
	US 6008255	A	19991228	US 1995-471305	19950606 <--
	US 6022900	A	20000208	US 1995-471919	19950606 <--
	US 6180676	B1	20010130	US 1995-472003	19950606 <--
	US 6248787	B1	20010619	US 1995-479050	19950606 <--
	US 5854289	A	19981229	US 1996-632305	19960415 <--
	US 2002028851	A1	20020307	US 2001-824217	20010403 <--
PRAI	US 1994-184540	B2	19940121 <--		
	US 1994-315170	A	19940929 <--		
	EP 1995-910110	A3	19950119 <--		
	WO 1995-US828	W	19950119 <--		
	US 1995-463568	A3	19950605 <--		
	US 1995-479050	A1	19950606 <--		

OS MARPAT 126:211914

GI



I

AB Title compds., e.g. [I; X2 = H, Q1, Q2; X1, X11, X21 = Q1, Q2; Z = NHCONH, C6H4, C5NH3, A(CH2)nA; n = 2-10; A = NHCO, NHCONH, NH, O; Q1 = H2N(CNH)NHN:CH, H2N(CNH)NHN:CMe], were prepd. Thus, N,N'-bis(3,5-diacetylphenyl)decanediamide (prepn. given), aminoguanidine hydrochloride, and aminoguanidine dihydrochloride were heated in EtOH for 18 h to give N,N'-bis(3,5-diacetylphenyl)decanediamide tetrakis(amidinohydrazone) tetrahydrochloride. The latter at 200 .mu.M gave 100% inhibition of urea prodn., NO2/NO3 prodn., and arginine transport in activated macrophages.

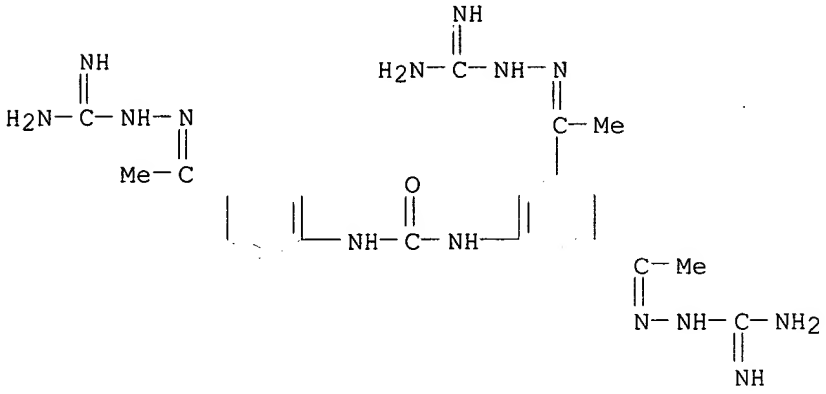
IT **169764-82-3P 169765-12-2P 169765-13-3P**
187959-61-1P
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of arylamidinohydrazones for treatment of cachexia and nitric oxide-mediated diseases)

IT **169765-14-4P 169765-32-6P 169765-36-0P**
169765-37-1P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. of arylamidinohydrazones for treatment of cachexia and nitric oxide-mediated diseases)

IT **169764-82-3P**
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of arylamidinohydrazones for treatment of cachexia and nitric oxide-mediated diseases)

RN 169764-82-3 HCAPLUS

CN Hydrazinecarboximidamide, 2,2'-[[5-[[[[4-[1-[(aminoiminomethyl)hydrazono]ethyl]phenyl]amino]carbonyl]amino]-1,3-phenylene]diethylidyne]bis-, trihydrochloride (9CI) (CA INDEX NAME)



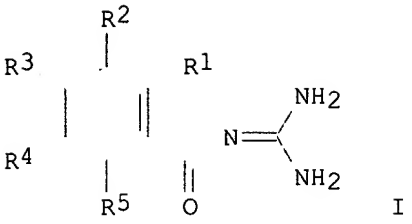
● 3 HCl

L74 ANSWER 13 OF 15 HCAPLUS COPYRIGHT 2002 ACS
AN 1995:662389 HCAPLUS
DN 123:55495
TI Preparation of ureiodobenzoylguanidines as sodium-proton antiporter inhibitors
IN Schwark, Jan-Robert; Lang, Hans-Jochen; Kleemann, Heinz-Werner; Weichert, Andreas; Scholz, Wolfgang; Albus, Udo
PA Hoechst A.-G., Germany
SO Eur. Pat. Appl., 17 pp.
CODEN: EPXXDW
DT Patent
LA German
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
PI	EP 638548	A1	19950215	EP 1994-112383	19940808	<--
	EP 638548	B1	19980422			
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE					
	DE 4327244	A1	19950216	DE 1993-4327244	19930813	<--
	TW 388753	B	20000501	TW 1994-83106270	19940711	<--
	AT 165342	E	19980515	AT 1994-112383	19940808	<--
	ES 2115115	T3	19980616	ES 1994-112383	19940808	<--
	FI 9403716	A	19950214	FI 1994-3716	19940811	<--
	AU 9470223	A1	19950223	AU 1994-70223	19940811	<--
	AU 683273	B2	19971106			
	CN 1111618	A	19951115	CN 1994-109503	19940811	<--
	CN 1060763	B	20010117			
	US 5559153	A	19960924	US 1994-289674	19940811	<--
	IL 110625	A1	19990312	IL 1994-110625	19940811	<--
	CA 2130031	AA	19950214	CA 1994-2130031	19940812	<--
	NO 9402985	A	19950214	NO 1994-2985	19940812	<--
	JP 07076566	A2	19950320	JP 1994-189725	19940812	<--
	ZA 9406074	A	19950320	ZA 1994-6074	19940812	<--
	HU 71816	A2	19960228	HU 1994-2346	19940812	<--
	HU 217628	B	20000328			
PRAI	DE 1993-4327244	A	19930813	<--		

OS MARPAT 123:55495

GI



AB Title compds. [I; 1 of R1,R3,R4 = NR6C(:X)NR7R8 and the others = H, halo, alk(en)yl(oxy), etc.; R6-R8 = H, (perfluoro)alkyl, alkenyl, etc.] were prepd. Thus, 5-chloroisatoic anhydride was condensed with N-trimethylsilylpiperidine and the product condensed with (H2N)2C:NH to give I (R1 = piperidinocarbonylamino, R2 = R3 = R5 = H, R4 = Cl) which had IC50 of 1-2.mu.M against rabbit erythrocyte Na+/H+-exchangers in vitro.

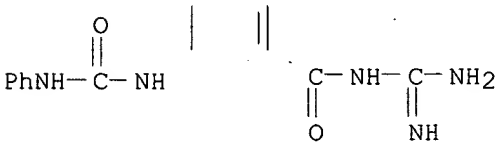
IT **164653-11-6P 164653-17-2P 164653-23-0P**
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of ureiodobenzoylguanidines as sodium-proton antiporter inhibitors)

IT **164653-32-1P 164653-36-5P 164653-41-2P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. of ureiodobenzoylguanidines as sodium-proton antiporter inhibitors)

IT **164653-11-6P**
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of ureiodobenzoylguanidines as sodium-proton antiporter inhibitors)

RN 164653-11-6 HCAPLUS

CN Benzamide, N-(aminoiminomethyl)-3-[[(phenylamino)carbonyl]amino]-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

L74 ANSWER 14 OF 15 HCAPLUS COPYRIGHT 2002 ACS

AN 1987:477448 HCAPLUS

DN 107:77448

TI Preparation of isophthalonitrile derivatives as agricultural bactericides

IN Ishikawa, Nobuo; Motoyoshi, Masatoshi

PA SDS Biotech Corp., Japan

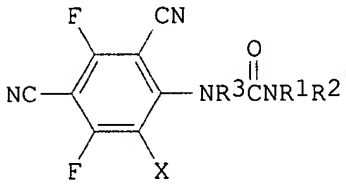
SO Jpn. Kokai Tokkyo Koho, 10 pp.
CODEN: JKXXAF

DT Patent

LA Japanese
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	JP 62081361	A2	19870414	JP 1985-220167	19851004 <--

OS CASREACT 107:77448
GI



I

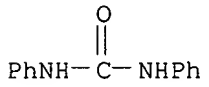
AB The title compds. I [X = Cl, F; R1, R2, R3 = H, alkyl, (un)substituted Ph], useful as agricultural antimicrobial agents, are prepd. A soln. of 2.00 g tetrafluoroisophthalonitrile and 1.11 g H2NCONHMe in 1,4-dioxane was refluxed for 12 h to give 80.7% I (R1 = Me; R2 = R3 = H; X = F), whose MIC (ppm) against Penicillium funiculosum, Aspergillus niger, Fusarium **proliferatum**, Gliocladium virens, and Rhizopus stolonifer are 50, 50, 50, 100, and 50, resp., vs. 5, 5, 500, >500, and 500 ppm for chlorothalonil.

IT **102-07-8**
RL: RCT (Reactant)
(arylation of, with tetrafluoroisophthalonitrile)

IT **109678-91-3P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as agricultural bactericide and fungicide)

IT **102-07-8**
RL: RCT (Reactant)
(arylation of, with tetrafluoroisophthalonitrile)

RN 102-07-8 HCAPLUS
CN Urea, N,N'-diphenyl- (9CI) (CA INDEX NAME)



L74 ANSWER 15 OF 15 HCAPLUS COPYRIGHT 2002 ACS
AN 1986:626077 HCAPLUS
DN 105:226077
TI Benzoylurea compounds and **antitumor** compositions containing them
IN Haga, Takahiro; Yamada, Nobutoshi; Sugi, Hideo; Koyanagi, Toru; Kondo, Nobuo; Nakajima, Tsunetaka; Watanabe, Masahiro; Yokoyama, Kazumasa
PA Ishihara Sangyo Kaisha, Ltd., Japan
SO Eur. Pat. Appl., 32 pp.
CODEN: EPXXDW
DT Patent
LA English
FAN.CNT 3

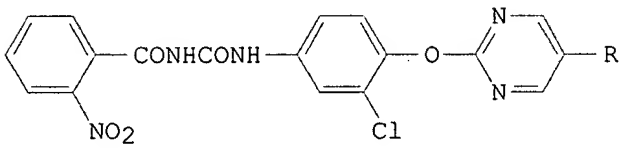
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 192235	A1	19860827	EP 1986-102063	19860218 <--
	EP 192235	B1	19891123		

R: BE, CH, DE, FR, GB, IT, LI, NL, SE

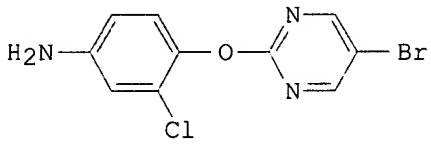
	JP 61191623	A2	19860826	JP 1985-32365	19850220 <--
	JP 61205257	A2	19860911	JP 1985-44737	19850308 <--
	JP 01056065	B4	19891128		
	US 4727077	A	19880223	US 1986-823521	19860129 <--
	US 4849425	A	19890718	US 1986-824088	19860130 <--
	ZA 8600775	A	19861029	ZA 1986-775	19860203 <--
	GB 2171695	A1	19860903	GB 1986-2792	19860205 <--
	GB 2171695	B2	19890105		
	AU 8653285	A1	19860911	AU 1986-53285	19860206 <--
	AU 593233	B2	19900208		
	CA 1266473	A1	19900306	CA 1986-501576	19860211 <--
	CA 1260396	A1	19890926	CA 1986-501662	19860212 <--
	FR 2577551	A1	19860822	FR 1986-2147	19860218 <--
	FR 2577551	B1	19880415		
	DD 243025	A5	19870218	DD 1986-287134	19860218 <--
	CH 671576	A	19890915	CH 1986-642	19860218 <--
	CN 86101087	A	19870225	CN 1986-101087	19860219 <--
	CN 1013196	B	19910717		
	ES 552191	A1	19870801	ES 1986-552191	19860219 <--
	SU 1500156	A3	19890807	SU 1986-4023808	19860219 <--
	DK 8600802	A	19860821	DK 1986-802	19860220 <--
	DK 163124	B	19920120		
	DK 163124	C	19920609		
	BR 8603945	A	19880517	BR 1986-3945	19860819 <--
PRAI	JP 1985-32365		19850220 <--		
	JP 1985-44737		19850308 <--		

OS CASREACT 105:226077

GI



I



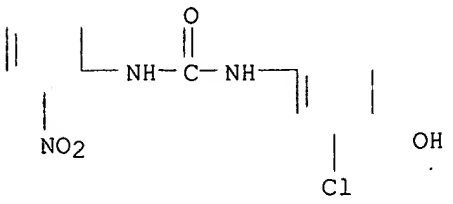
II

AB Title compds. I (R = Br, Cl) were prepd. as **antitumor** agents. Thus, 5-bromo-2-chloropyrimidine and 2,4-Cl(H2N)C6H3OH were condensed in Me2SO contg. K2CO3 to give pyrimidinyloxyaniline II, which was treated with 2-O2NC6H4CONCO to give I (R = Br) (III). I (R = Cl) (IV) was similarly prepd., and III was also prepd. by 2 other methods. Against leukemia P-388 in mice, III and IV showed i.p. activity inferior or comparable to the known compd. I (R = iodo), but showed markedly superior oral activity. A liposomal formulation was prepd. from III 5, yolk phospholipid 2, .alpha.-tocopherol 0.001, and physiol. saline 92.999 wt. parts.

IT **105355-39-3P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and condensation of, with bromochloropyrimidine)

IT **105355-39-3P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and condensation of, with bromochloropyrimidine)

RN 105355-39-3 HCAPLUS
CN Urea, N-(3-chloro-4-hydroxyphenyl)-N'-(2-nitrophenyl)- (9CI) (CA INDEX NAME)



=> d his

(FILE 'HOME' ENTERED AT 10:57:31 ON 02 MAY 2002)
SET COST OFF

FILE 'REGISTRY' ENTERED AT 10:57:51 ON 02 MAY 2002
ACT KUMAR776/A

L1 STR
L2 23426 SEA FILE=REGISTRY SSS FUL L1

L3 2 S L2 AND C22H23N3O2/MF
L4 23424 S L2 NOT L3

FILE 'HCAPLUS' ENTERED AT 10:58:50 ON 02 MAY 2002
L5 8315 S L4

FILE 'REGISTRY' ENTERED AT 11:00:54 ON 02 MAY 2002
L6 1 S 144378-33-6

FILE 'HCAPLUS' ENTERED AT 11:01:43 ON 02 MAY 2002
L7 297 S L6
L8 546 S RAF KINASE OR C RAF KINASE OR PROTEIN KINASE C RAF OR GENE C
L9 17 S KINASE PHOSPHORYLATING GENE C RAF PROTEIN
L10 574 S L7-L9
L11 7 S L5 AND L10

FILE 'REGISTRY' ENTERED AT 11:03:31 ON 02 MAY 2002
L12 11 S (L8 OR L9) NOT L6

FILE 'HCAPLUS' ENTERED AT 11:04:15 ON 02 MAY 2002
L13 143 S L12
L14 1 S L5 AND L13
L15 7 S L11,L14
L16 6950 S L5 AND (PY<=1997 OR PRY<=1997 OR AY<=1997)
L17 5 S L15 AND L16
E BAYER/PA,CS
L18 197 S E3,E4 AND L5
E MILLER S/AU
L19 930 S E3-E36
E MILLER SCOTT/AU
L20 222 S E3-E26
E OSTERHOUT M/AU
L21 34 S E3-E5,E7-E9
E DUMAS J/AU
L22 458 S E3-E16
E KHIRE U/AU

```
L23          24 S E4-E6
                E LOWINGER T/AU
L24          23 S E4-E6
                E RIEDL B/AU
L25          84 S E3,E7
                E SCOTT W/AU
L26         155 S E3,E22-E27
                E SCOTT WILL/AU
L27         153 S E3,E34-E39
                E SMITH R/AU
L28         992 S E3-E15
                E SMITH ROGER/AU
L29         219 S E3-E7
                E WOOD J/ AU
L30         178 S E3,E16-E20
                E WOOD JILL/AU
L31          14 S E3-E5
                E GUNN D/AU
L32          33 S E3,E6,E15,E16
                E RODRIGUEZ M/AU
L33         942 S E3-E70,E242-E251
                E WANG M/AU
L34        1245 S E3-E34
                E WANG MING/AU
L35        2083 S WANG MING?/AU
                E TURNER T/AU
L36         358 S E3-E23
                E TURNER TIFFANY/AU
L37           1 S E3
                E BRENNAN C/AU
L38          74 S E3-E13,E21-E25
L39          18 S L5 AND L19-L38
L40          10 S L16 AND L39
                E GUNN DAVID/AU
L41          10 S E3
L42           3 S L41 AND L5
L43           2 S RODRIGUEZ M?/AU AND L5
L44           7 S L39,L42,L43,L18 AND L15
L45           5 S L16 AND L44
L46           2 S L44 NOT L45

     FILE 'REGISTRY' ENTERED AT 11:14:47 ON 02 MAY 2002

     FILE 'HCAPLUS' ENTERED AT 11:15:08 ON 02 MAY 2002
                SEL HIT RN L44

     FILE 'REGISTRY' ENTERED AT 11:16:11 ON 02 MAY 2002
L47         332 S E1-E332
L48           2 S L47 AND L6,L12
L49         330 S L47 NOT L48

     FILE 'REGISTRY' ENTERED AT 11:16:56 ON 02 MAY 2002
                SAV L49 KUMAR776A/A
L50       23094 S L4 NOT L49

     FILE 'HCAPLUS' ENTERED AT 11:17:55 ON 02 MAY 2002
L51        8301 S L50
L52        6940 S L16 AND L51
L53        1728 S L52 AND (1 OR 63)/SC,SX
                E ANTITUMOR/CT
                E E5+ALL
L54         303 S L52 AND E4,E3+NT
```

FILE 'HCAPLUS' ENTERED AT 11:38:35 ON 02 MAY 2002

L55 643 S L52 AND (?NEOPLAS? OR ?CANCER? OR ?CARCIN? OR ?TUMOR? OR ?TUM
L56 645 S L54,L55
L57 519 S L53 AND L56
L58 134 S L57 AND P/DT
L59 91 S L58 AND US/PC
L60 44 S L57 AND ?KINASE?
L61 19 S L60 AND L58
L62 1033 S L50 (L) THU/RL
L63 218 S L62 AND L57
L64 97 S L63 AND L58
L65 69 S L64 AND L59
L66 8 S L65 AND L60
L67 19 S L61,L66

FILE 'HCAPLUS' ENTERED AT 11:43:30 ON 02 MAY 2002

L68 262 S BENZEN?/SC AND L52
L69 79 S L68 AND L53
L70 11 S L68 AND L54
L71 16 S L68 AND L56
L72 13 S L68 AND L63
L73 15 S L69 AND L70-L72
L74 15 S L70-L73 NOT L67

US 097769360JP1

Creation date: 04-22-2004
Indexing Officer: JACKERMANWILSON - JEAN ACKERMAN-WILSON
Team: OIPEBackFileIndexing
Dossier: 09776936

Legal Date: 05-07-2002

No.	Doccode	Number of pages
1	SRNT	4

Total number of pages: 4

Remarks:

Order of re-scan issued on .....